* * * * * * * * * * Welcome to STN International * * * * * * * * * *

| | | |
|---|---|---|
| NEWS 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS 2 | | "Ask CAS" for self-help around the clock |
| NEWS 3 | May 12 | EXTEND option available in structure searching |
| NEWS 4 | May 12 | Polymer links for the POLYLINK command completed in REGISTRY |
| NEWS 5 | May 27 | New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus |
| NEWS 6 | May 27 | CAplus super roles and document types searchable in REGISTRY |
| NEWS 7 | Jun 28 | Additional enzyme-catalyzed reactions added to CASREACT |
| NEWS 8 | Jun 28 | ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG, and WATER from CSA now available on STN(R) |
| NEWS 9 | Jul 12 | BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS |
| NEWS 10 | Jul 30 | BEILSTEIN on STN workshop to be held August 24 in conjunction with the 228th ACS National Meeting |
| NEWS 11 | AUG 02 | IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields |
| NEWS 12 | AUG 02 | CAplus and CA patent records enhanced with European and Japan Patent Office Classifications |
| NEWS 13 | AUG 02 | STN User Update to be held August 22 in conjunction with the 228th ACS National Meeting |
| NEWS 14 | AUG 02 | The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available |
| NEWS 15 | AUG 04 | Pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! will change September 1, 2004 |

| | |
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| NEWS EXPRESS | JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004 |
| NEWS HOURS | STN Operating Hours Plus Help Desk Availability |
| NEWS INTER | General Internet Information |
| NEWS LOGIN | Welcome Banner and News Items |
| NEWS PHONE | Direct Dial and Telecommunication Network Access to STN |
| NEWS WWW | CAS World Wide Web Site (general information) |

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FILE 'HOME' ENTERED AT 15:38:42 ON 26 AUG 2004

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 15:38:49 ON 26 AUG 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file

h eb c g cg b cg eb

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STRUCTURE FILE UPDATES: 25 AUG 2004 HIGHEST RN 732955-11-2
DICTIONARY FILE UPDATES: 25 AUG 2004 HIGHEST RN 732955-11-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

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SAMPLE SCREEN SEARCH COMPLETED - 7718 TO ITERATE

13.0% PROCESSED 1000 ITERATIONS 8 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 149095 TO 159625
PROJECTED ANSWERS: 763 TO 1705

L2 8 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
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FULL SCREEN SEARCH COMPLETED - 153893 TO ITERATE

100.0% PROCESSED 153893 ITERATIONS 813 ANSWERS
SEARCH TIME: 00.00.05

L3 813 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY 162.98 TOTAL SESSION 163.19

FULL ESTIMATED COST

FILE 'HCAPLUS' ENTERED AT 15:50:21 ON 26 AUG 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


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FILE COVERS 1907 - 26 Aug 2004 VOL 141 ISS 9
FILE LAST UPDATED: 25 Aug 2004 (20040825/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 28 L3

=> s l4 and lu, z?/au
5751 LU, Z?/AU
L5 3 L4 AND LU, Z?/AU

=> d l5, ibib abs fhitstr, 1-3

L5 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:511307 HCAPLUS
DOCUMENT NUMBER: 139:85368
TITLE: Preparation of barbituric acids as inhibitors of TNF-α converting enzyme (TACE), aggrecanase and/or matrix metalloproteinases
INVENTOR(S): Duan, Jingwu; Jiang, Bin; Chen, Lihua; **Lu, Zhonghui**; Barbosa, Joseph; Pitts, William
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003053941 | A2 | 20030703 | WO 2002-US40458 | 20021217 |
| WO 2003053941 | A3 | 20030814 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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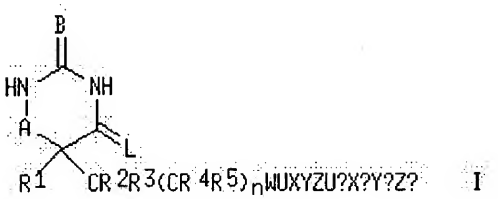
US 2003229084 A1 20031211 US 2002-321144 20021217
PRIORITY APPLN. INFO.: US 2001-342658P P 20011220
OTHER SOURCE(S): MARPAT 139:85368
GI



I

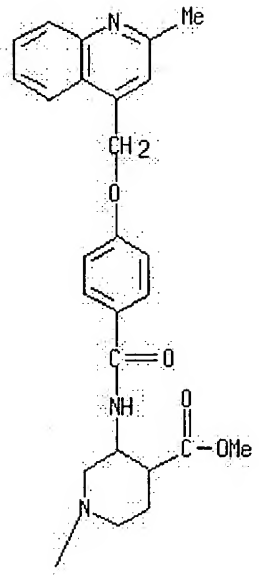
AB The present application describes novel barbituric acid derivs. (shown as I; variables defined below; e.g. 5-methyl-5-[3-[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]-3-oxopropyl]-2,4,6(1H,3H,5H)-pyrimidinetrione) or pharmaceutically acceptable salt or prodrug forms thereof, which are useful as TNF-α converting enzyme (TACE), aggrecanase and matrix metalloproteinases (MMP) inhibitors. Although the methods of prepn. are not claimed, 60 example prepns. are included. Some examples of I (specific compds. not stated) inhibit matrix metalloproteinases with Ki ≤10 μM. For I: A is C(O), C(S) or CH2; B is O or S; L is O or S; W = (CRaRa1)m, C2-3 alkenylene, and C2-3 alkynylene; U = C(O), CRa(OH), C(O)O, OC(O), C(O)NRa1, NRa1C(O), OC(O)O, OC(O)NRa1, NRa1C(O)O, and NRa1C(O)NRa1; X is absent or C1-3 alkylene, C2-3 alkenylene, and C2-3 alkynylene; Y is absent or O, NRa1, S(O)p, and C(O); Z = C3-13 carbocycle substituted with 0-5 Rb, and a 5-14 membered heterocycle comprising C atoms and 1-4 heteroatoms N, O, and S(O)p, and substituted with 0-5 Rb; Ua is absent or O, NRa1, C(O), CRa(OH), C(O)O, OC(O), C(O)NRa1, NRa1C(O), OC(O)O, OC(O)NRa1, NRa1C(O)O, NRa1C(O)NRa1, S(O)p, S(O)pNRa1, NRa1S(O)p, and NRa1SO2NRa1; Xa is absent or C1-10-alkylene, C2-10 alkenylene, and C2-10 alkynylene; Ya is absent or O, NRa1, S(O)p, and C(O); Za = C3-13 carbocycle substituted with 0-5 Rc and a 5-14 membered heterocycle comprising C atoms and 1-4 heteroatoms N, O, and S(O)p, and substituted with 0-5 Rc. R1 = CHF2, CH2F, CF3, C1-6 alkylene-Q (Q = H, CF3, etc.), etc.; R2 = Q1 (Q1 = H, carbocyclyl, heterocyclyl), C1-6 alkylene-Q1, etc.; R3 = Q, C1-6 alkylene-Q, etc.; R4, R5 = H, C1-6 alkyl, etc.; addnl. details including provisos are given in the claims.

IT **554451-88-6**, 3-[[4-[(2-Methylquinolin-4-yl)methoxy]benzoyl]amino]piperidine-1,4-dicarboxylic acid 1-tert-butyl ester 4-methyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of barbituric acids as inhibitors of TNF-α converting enzyme, aggrecanase and/or matrix metalloproteinases)

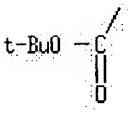
RN 554451-88-6 HCAPLUS
CN 1,4-Piperidinedicarboxylic acid, 3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, 1-(1,1-dimethylethyl) 4-methyl ester (9CI) (CA INDEX NAME)

h eb c g cg b cg eb

PAGE 1-A




PAGE 2-A




L5 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:242278 HCAPLUS
DOCUMENT NUMBER: 138:271682
TITLE: Preparation of cyclic hydroxamic acids as inhibitors of matrix metalloproteinases and/or TNF-α converting enzyme for treatment of inflammatory disorders
INVENTOR(S): Ott, Gregory; Chen, Xiao-Tao; Duan, Jingwu; **Lu, Zhonghui**
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 344 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003024899 | A2 | 20030327 | WO 2002-US29685 | 20020916 |
| WO 2003024899 | A3 | 20031127 | | |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,

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CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| US 2003139388 | A1 | 20030724 | US 2002-244626 | 20020916 |
| US 6740649 | B2 | 20040525 | | |
| EP 1427408 | A2 | 20040616 | EP 2002-775865 | 20020916 |

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| PRIORITY APPLN. INFO.: | US 2001-322630P | P | 20010917 |
| | WO 2002-US29685 | W | 20020916 |

OTHER SOURCE(S): MARPAT 138:271682

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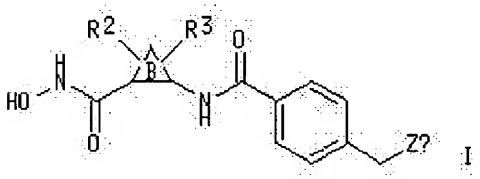

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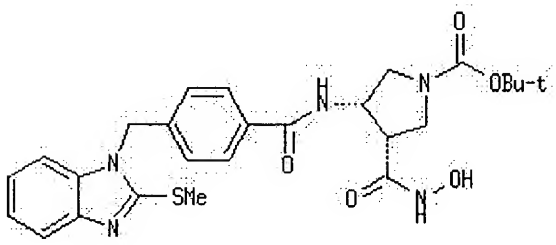

II

AB Title compds. I [wherein ring B = (un)substituted 4-7 membered (hetero)cyclic ring contg. 0-2 O, N, NR1, or SOp atoms and 0-3 carbonyl groups; R1 and R2 = independently Q, alk(en/yn)ylene-Q, or (un)substituted alkylene-Q interrupted by O, NRa, CO, CO2, CONRa, NRaCO, NRaCO2, NRaCONRa, SOp, NRaSO2, or SO2NRa; or R1 = (un)substituted alkylene-Q interrupted by OCO, OCO2, or OCONRa; Q = H or (un)substituted (hetero)cyclyl; R3 = Q1, Cl, F, alk(en/yn)ylene-Q1, or (un)substituted alkylene-Q1 interrupted by O, NR1, NRaCO, CONRa, CO, CO2, SOp, or SO2NRa; Q1 = H or (un)substituted Ph, naphthyl, or heterocyclyl; Za = (un)substituted benzimidazolyl, indolyl, imidazopyridinyl, pyrazolylpyridinyl, benzofuranyl, benzothiazinyl, quinolinyl, etc.; Ra = independently H, alkyl, Ph, or benzyl; p = 0-2; or stereoisomers or pharmaceutically acceptable salts thereof] were prepd. as inhibitors of matrix metalloproteinases (MMP), TNF-a converting enzyme (TACE), aggrecanase, or a combination thereof. For example, reaction of benzyl Me maleate with paraformaldehyde and glycine gave benzyl Me (cis)-3,4-pyrrolidinedicarboxlyate (100%). BOC-protection (64%), debenzylation (96%), resoln. of the (3S,4S)-isomer with (S)-α-methylbenzylamine, conversion to the carbamate with DPPA and PhCH2OH (76%), and Pd catalyzed hydrogenation (100%) provided Me (3S,4S)-4-amino-1-(tert-butoxycarbonyl)-3-pyrrolidinecarboxylate. Coupling of the amine with 4-[(2-methylthio-1H-benzimidazol-1-yl)methyl]benzoic acid (prepn. given) afforded the amide (99%), which was treated with NH2OH•HCl/MeONa to give the hydroxamic acid (3S,4S)-II (33%). A no. of the compds. of the invention inhibited MMP-1, 2, 3, 7, 8, 9, 10, 12, 13, 14, 15, and/or 16 with Ki values of ≤ 10 μM. Thus, I are useful for the treatment of a wide variety of inflammatory disorders (no data).

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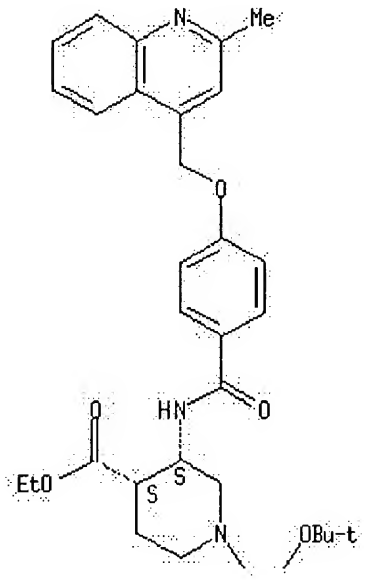
IT 362489-81-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of cyclic hydroxamic acids as MMP and/or TACE inhibitors for treatment of inflammatory disorders)
RN 362489-81-4 HCAPLUS
CN 1,4-Piperidinedicarboxylic acid, 3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, 1-(1,1-dimethylethyl) 4-ethyl ester, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A




PAGE 2-A


L5 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

| | |
|---|---|
| ACCESSION NUMBER: | 2001:713294 HCAPLUS |
| DOCUMENT NUMBER: | 135:257169 |
| TITLE: | Preparation of cyclic β-amino acid derivatives as inhibitors of matrix metalloproteases and TNF-α |
| INVENTOR(S): | Duan, Jingwu; Ott, Gregory; Chen, Linhua; **Lu, Zhonghui**; Maduskuie, Thomas P., Jr.; Voss, Matthew E.; Xue, Chu-Biao |
| PATENT ASSIGNEE(S): | Dupont Pharmaceuticals Company, USA |
| SOURCE: | PCT Int. Appl., 298 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 1 |
| PATENT INFORMATION: | |

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| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2001070673 | A2 | 20010927 | WO 2001-US8334 | 20010315 |
| WO 2001070673 | A3 | 20020314 | | |
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| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| EP 1263755 | A2 | 20021211 | EP 2001-924170 | 20010315 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR | | | | |
| BR 2001009467 | A | 20030603 | BR 2001-9467 | 20010315 |
| JP 2003528072 | T2 | 20030924 | JP 2001-568885 | 20010315 |
| EE 200200529 | A | 20040216 | EE 2002-529 | 20010315 |
| US 2002016336 | A1 | 20020207 | US 2001-811233 | 20010316 |
| US 6743807 | B2 | 20040601 | | |
| US 2004162426 | A1 | 20040819 | US 2004-779539 | 20040213 |
| PRIORITY APPLN. INFO.: | | | US 2000-190182P | P 20000317 |
| | | | US 2000-233373P | P 20000918 |
| | | | US 2000-255539P | P 20001214 |
| | | | WO 2001-US8334 | W 20010315 |
| | | | US 2001-811233 | A3 20010316 |

OTHER SOURCE(S): MARPAT 135:257169

AB Novel cyclic β-amino acid derivs. A-CRR2aCRR2bNR1CO-Z-Ua-Xa-Ya-Za [A = CO2H, CH2CO2H, SH, CH2SH, S(O)Ra:NH (Ra = H, alkyl, Ph, benzyl), P(O)(OH)2, etc.; CRCR is a substituted 3-13 membered nonarom. carbocyclic or heterocyclic ring; Z is absent or substituted C3-13 carbocycle or 5-14 membered heterocycle; Ua is absent or O, NRa1 (Ra1 = H, alkyl), CO, CO2, O2C, CONRa1, S(O)p (p = 0-2), etc.; Xa is absent or C1-10 alkylene, C2-10 alkenylene or alkynylene; Ya is absent or O, NRa1, S(O)p or CO; Za is H, substituted C3-13 carbocycle or 5-14 membered heterocycle; R1 is H, C1-4 alkyl, Ph, benzyl; R2a is H, C1-6 alkyl, ORa, NRaRa1 or S(O)pRa; R2b is H, C1-6 alkyl (with provisos)] or pharmaceutically acceptable salts were prepd. as metalloprotease and TNF-α inhibitors. Thus, (3S,4S)-N-hydroxy-1-isopropyl-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-3-pyrrolidinecarboxamide was prepd. by a multistep procedure starting with condensation of benzyl Me maleate, glycine, and paraformaldehyde to form 3,4-pyrroledicarboxylate diester and involving amidation of 4-[(2-methyl-4-quinolinyl)methoxy]benzoic acid.

IT **362485-48-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of cyclic β-amino acid derivs. as inhibitors of matrix metalloproteases and TNF-α)

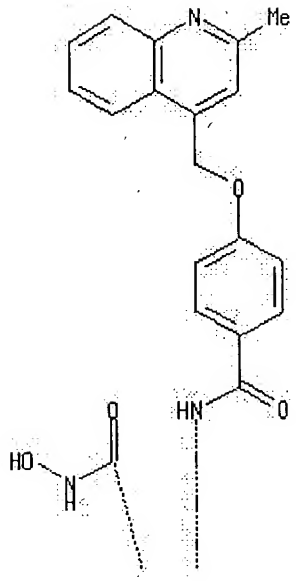
RN 362485-48-1 HCAPLUS

CN 1-Piperidinecarboxylic acid, 3-[(hydroxyamino)carbonyl]-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, 1,1-dimethylethyl ester, (3S,4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

h eb c g cg b cg eb

PAGE 1-A

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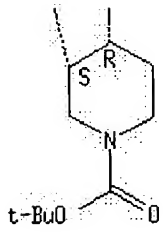


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L2              8 S L1
L3            813 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 15:50:21 ON 26 AUG 2004
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L5              3 S L4 AND LU, Z?/AU

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L6             25 L4 NOT L5

=> s l6 and maduskuie, t?/au
               33 MADUSKUIE, T?/AU
L7              4 L6 AND MADUSKUIE, T?/AU

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L7   ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2004 ACS on STN
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ACCESSION NUMBER:         2004:310829  HCAPLUS
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h eb c g cg b cg eb

DOCUMENT NUMBER: 140:303552
TITLE: Preparation of β-amino acid derivatives as inhibitors of matrix metalloproteases and TNF-α
INVENTOR(S): Duan, Jingwu; King, Bryan W.; Decicco, Carl; **Maduskuie, Thomas P.**; Voss, Mathew E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 150 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004072802 | A1 | 20040415 | US 2002-267207 | 20021009 |
| PRIORITY APPLN. INFO.: | | | US 2002-267207 | 20021009 |

OTHER SOURCE(S): MARPAT 140:303552

AB Novel β-amino acid derivs. A-CR3R4aCR2R4NR1CO-X-Z-Ua-Xa-Ya-Za [A = CO2H, SH, CH2SH, S(O)Ra:NH (Ra = H, alkyl), P(O)(OH)2, etc.; X, Xa is absent or alkylene, alkenylene or alkynylene; Z is absent or substituted C3-13 carbocycle or 5-14 membered heterocycle; Ua is absent or O, NRa1 [Ra1 = H, (un)substituted alkyl, alkenyl or alkynyl; Ra and Ra1 may form a ring], CO, CO2, O2C, CONRa1, S(O)p (p = 0-2), etc.; Ya is absent or O, NRa1, S(O)p or CO; Za is H, substituted C3-13 carbocycle or 5-14 membered heterocycle; R1 is H, alkyl, Ph, benzyl; R2 is Q (Q is H, substituted carbocycle or heterocycle), alkylene-Q, (CRaRa1)r1O(CRaRa1)r-Q (r, r1 = 0-4), (CRaRa1)r1NRa(CRaRa1)r-Q, etc.; R3 = Q1 (Q1 is any group given for Q), alkylene-Q1, (CRaRa1)r1O(CRaRa1)r-Q1, (CRaRa1)r1NRa(CRaRa1)r-Q1, etc.; R4, R4a = H, substituted alkyl, alkenyl or alkynyl; alternatively R1 and R2, R1 and R3, R3 and R4a may form rings (with provisos)] or a stereoisomer or pharmaceutically acceptable salt were prepd. as metalloprotease and TNF-α inhibitors. Thus, N-hydroxy-1-[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]acetyl]-3-azetidinecarboxamide was prepd. by a multistep procedure involving reactions of Me 4-hydroxyphenylacetate, 2-methyl-4-quinolinylmethanol, and 3-azetidinecarboxylic acid Me ester.

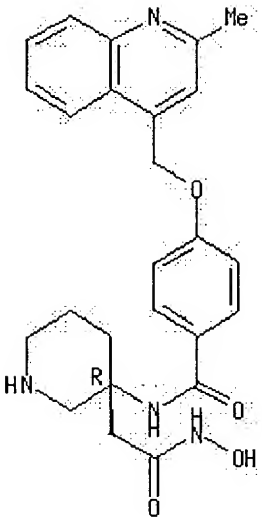
IT **362701-28-8P**
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of β-amino acid derivs. as inhibitors of matrix metalloproteases and TNF-α)

RN 362701-28-8 HCAPLUS
CN 3-Piperidineacetamide, N-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3R)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

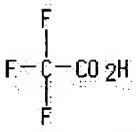
CRN 362701-27-7
CMF C25 H28 N4 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L7 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:444499 HCAPLUS
DOCUMENT NUMBER: 137:33207
TITLE: Preparation of novel N-substituted-γ,γ-trisubstituted lactam derivatives as matrix metalloproteinase inhibitors
INVENTOR(S): Duan, Jingwu; DeCicco, Carl P.; Wasserman, Zelda R.; **Maduskuie, Thomas P., Jr.**
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 119 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6403632 | B1 | 20020611 | US 2000-516709 | 20000301 |
| US 2003134827 | A1 | 20030717 | US 2002-96619 | 20020312 |
| US 6610731 | B2 | 20030826 | | |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1997-62418P | P | 19971003 |
| US 1998-165747 | A3 | 19981002 |
| US 2000-516709 | A3 | 20000301 |

OTHER SOURCE(S): MARPAT 137:33207
GI

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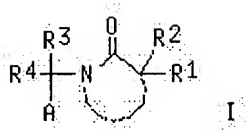

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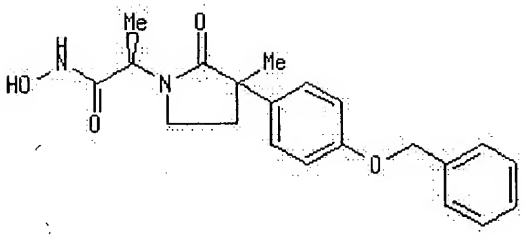


II

AB Title compds. [I; A is selected from COOH, CH2COOH, CONHOH, SH, CH2SH, PO(OH)2, etc.; ring B is a 4-8 membered cyclic amide contg. 0-3 heteroatoms from O, N, and S, etc.; R1 is phenylmethoxyphenyl, phenoxyphenyl, etc.; R2 is H, CH3, Et, i-Pr, etc.; R1-R2 combine to form heterocyclic; R3 is H, alkylene, heterocyclic, etc.; R4 is H, alkylene, etc.; R3-R4 combine to form heterocyclic], stereoisomer, and pharmaceutically acceptable salt thereof are prepd. as useful metalloprotease inhibitors. For instance, 4-benzyloxyphenyl acetate was sequentially alkylated (THF, NaHMDS) with MeI and allyl bromide to afford the α,α-bis(alkylated) deriv. which was converted to the aldehyde (CH2Cl2, O3) and was subsequently reacted with D-alanine Me ester hydrochloride and Zn° in HOAc to yield the lactam ester. This intermediate was treated with hydroxylamine to give hydroxamic acid II.

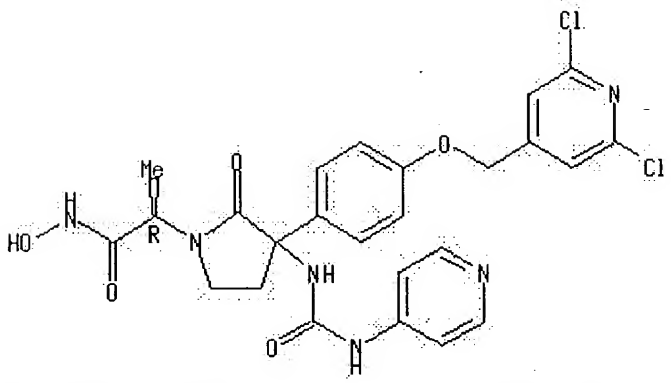
IT **223403-20-1P**, 1-Pyrrolidineacetamide, 3-[4-[(2,6-dichloro-4-pyridinyl)methoxy]phenyl]-N-hydroxy-α-methyl-2-oxo-3-[[(4-pyridinylamino)carbonyl]amino]-, (αR)-
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(N-γ,γ-trisubstituted lactam derivs. as MMP-3/aggrecanase inhibitors)

RN 223403-20-1 HCAPLUS

CN 1-Pyrrolidineacetamide, 3-[4-[(2,6-dichloro-4-pyridinyl)methoxy]phenyl]-N-hydroxy-α-methyl-2-oxo-3-[[(4-pyridinylamino)carbonyl]amino]-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

h eb c g cg b cg eb



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:713343 HCAPLUS
DOCUMENT NUMBER: 135:272894
TITLE: Preparation of β-amino acid derivatives as inhibitors of matrix metalloproteases and TNF-α
INVENTOR(S): Duan, Jingwu; King, Bryan W.; Decicco, Carl; **Maduskuie, Thomas P., Jr.**; Voss, Matthew E.
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 483 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001070734 | A2 | 20010927 | WO 2001-US8336 | 20010315 |
| WO 2001070734 | A3 | 20020314 | | |
| W: AT, AU, BR, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HU, IL, IN, JP, KR, LT, LU, LV, NZ, PL, PT, RO, SE, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| AU 2001050850 | A5 | 20011003 | AU 2001-50850 | 20010315 |
| EP 1263756 | A2 | 20021211 | EP 2001-924171 | 20010315 |
| EP 1263756 | B1 | 20040225 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR | | | | |
| BR 2001009469 | A | 20030429 | BR 2001-9469 | 20010315 |
| JP 2003528097 | T2 | 20030924 | JP 2001-568935 | 20010315 |
| AT 260272 | E | 20040315 | AT 2001-924171 | 20010315 |
| US 2002013341 | A1 | 20020131 | US 2001-811116 | 20010316 |
| US 6495565 | B2 | 20021217 | | |
| PRIORITY APPLN. INFO.: | | | US 2000-190183P P | 20000317 |
| | | | US 2000-235467P P | 20000926 |
| | | | US 2000-252062P P | 20001120 |
| | | | WO 2001-US8336 W | 20010315 |

OTHER SOURCE(S): MARPAT 135:272894

AB Novel β-amino acid derivs. A-CR3R4aCR2R4NR1CO-X-Z-Ua-Xa-Ya-Za [A = CO2H, SH, CH2SH, S(O)Ra:NH (Ra = H, alkyl), P(O)(OH)2, etc.; X, Xa is absent or alkylene, alkenylene or alkynylene; Z is absent or substituted

h eb c g cg b cg eb

C3-13 carbocycle or 5-14 membered heterocycle; Ua is absent or O, NRa1 [Ra1 = H, (un)substituted alkyl, alkenyl or alkynyl; Ra and Ra1 may form a ring], CO, CO2, O2C, CONRa1, S(O)p (p = 0-2), etc.; Ya is absent or O, NRa1, S(O)p or CO; Za is H, substituted C3-13 carbocycle or 5-14 membered heterocycle; R1 is H, alkyl, Ph, benzyl; R2 is Q (Q is H, substituted carbocycle or heterocycle), alkylene-Q, (CRaRa1)r1O(CRaRa1)r-Q (r, r1 = 0-4), (CRaRa1)r1NRa(CRaRa1)r-Q, etc.; R3 = Q1 (Q1 is any group given for Q), alkylene-Q1, (CRaRa1)r1O(CRaRa1)r-Q1, (CRaRa1)r1NRa(CRaRa1)r-Q1, etc.; R4, R4a = H, substituted alkyl, alkenyl or alkynyl; alternatively R1 and R2, R1 and R3, R3 and R4a may form rings (with provisos)] or a stereoisomer or pharmaceutically acceptable salt were prepd. as metalloprotease and TNF-α inhibitors. Thus, N-hydroxy-1-[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]acetyl]-3-azetidinecarboxamide was prepd. by a multistep procedure involving reactions of Me 4-hydroxyphenylacetate, 2-methyl-4-quinolinylmethanol, and 3-azetidinecarboxylic acid Me ester.

IT **362701-28-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of β-amino acid derivs. as inhibitors of matrix metalloproteases and TNF-α)

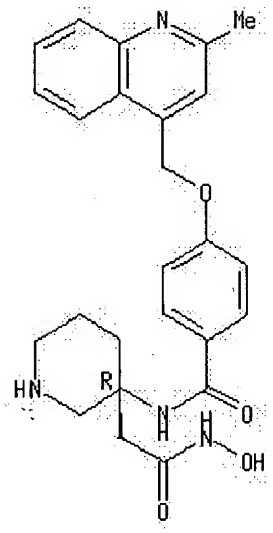
RN 362701-28-8 HCAPLUS

CN 3-Piperidineacetamide, N-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3R)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 362701-27-7
CMF C25 H28 N4 O4

Absolute stereochemistry.




CM 2

CRN 76-05-1
CMF C2 H F3 O2

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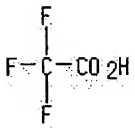

L7 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:244635 HCAPLUS
DOCUMENT NUMBER: 130:296611
TITLE: Preparation of novel lactam as metalloprotease inhibitors
INVENTOR(S): Duan, Jinguw; Decicco, Carl P.; Wasserman, Zelda R.; **Maduskuie, Thomas P., Jr.**
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 333 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 9918074 | A1 | 19990415 | WO 1998-US21037 | | 19981002 |
| W: AU, BR, CA, CN, CZ, EE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | | |
| ZA 9808967 | A | 20000403 | ZA 1998-8967 | | 19981001 |
| CA 2305679 | AA | 19990415 | CA 1998-2305679 | | 19981002 |
| AU 9896866 | A1 | 19990427 | AU 1998-96866 | | 19981002 |
| AU 747239 | B2 | 20020509 | | | |
| US 6057336 | A | 20000502 | US 1998-165747 | | 19981002 |
| EP 1027332 | A1 | 20000816 | EP 1998-950954 | | 19981002 |
| EP 1027332 | B1 | 20040526 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | | |
| BR 9815398 | A | 20001031 | BR 1998-15398 | | 19981002 |
| EE 200000199 | A | 20010416 | EE 2000-200000199 | | 19981002 |
| JP 2001519331 | T2 | 20011023 | JP 2000-514886 | | 19981002 |
| TW 541304 | B | 20030711 | TW 1998-87116499 | | 19981021 |
| NO 2000000783 | A | 20000529 | NO 2000-783 | | 20000217 |
| PRIORITY APPLN. INFO.: | | | US 1997-62418P | P | 19971003 |
| | | | WO 1998-US21037 | W | 19981002 |

OTHER SOURCE(S): MARPAT 130:296611
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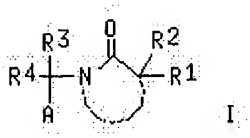

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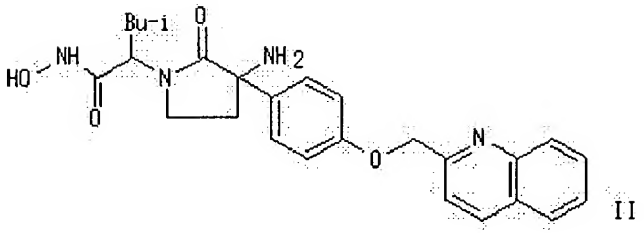


II

AB Title compds. [I; A is selected from COOH, CH2COOH, CONHOH, SH, CH2SH, PO(OH)2, etc.; ring B is a 4-8 membered cyclic amide contg. 0-3 heteroatoms from O, N, and S, etc.; R1 is phenylmethoxyphenyl, phenoxyphenyl, etc.; R2 is H, CH3, Et, i-Pr, etc.; R1-R2 combine to form heterocyclic; R3 is H, alkylene, heterocyclic, etc.; R4 is H, alkylene, etc.; R3-R4 combine to form heterocyclic], stereoisomer, and pharmaceutically acceptable salt thereof are prepd. as useful metalloprotease inhibitors. Thus, compd. II was prepd. via alkylation, oxidn., amination, and cyclization.

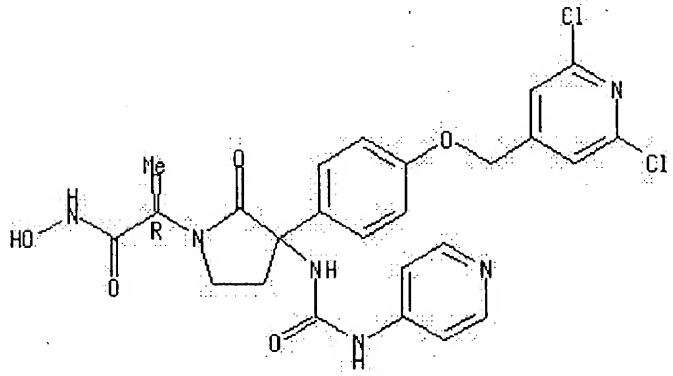
IT **223403-20-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel lactam metalloprotease inhibitors)

RN 223403-20-1 HCAPLUS

CN 1-Pyrrolidineacetamide, 3-[4-[(2,6-dichloro-4-pyridinyl)methoxy]phenyl]-N-hydroxy-α-methyl-2-oxo-3-[[(4-pyridinylamino)carbonyl]amino]-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2               8 S L1
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L7               4 S L6 AND MADUSKUIE, T?/AU

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L8              21 L6 NOT L7

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L10  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2002:927249 HCAPLUS
DOCUMENT NUMBER: 138:14059
TITLE: Preparation of spiro-fused hydantoin derivatives as inhibitors of matrix metalloproteinases
INVENTOR(S): Sheppeck, James E.; Duan, Jingwu; **Xue, Chu-Biao**; Wasserman, Zelda
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 350 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002096426 | A1 | 20021205 | WO 2002-US16381 | 20020523 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
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| US 2003130273 | A1 | 20030710 | US 2002-155575 | 20020523 |
| EP 1397137 | A1 | 20040317 | EP 2002-741724 | 20020523 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |

| PRIORITY APPLN. INFO.: | | | |
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| US 2001-293571P | P | 20010525 | |
| WO 2002-US16381 | W | 20020523 | |

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OTHER SOURCE(S): MARPAT 138:14059
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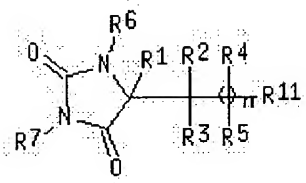


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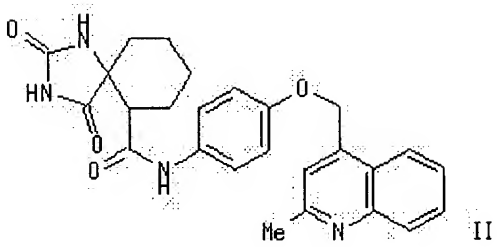



II

AB Title compds. I [R11 = W-U-X-Y-Z-Ua-Xa-Ya-Za; W = alkyl, alkenylene, alkynylene; U = absent, amino, CO, alkyl, carboxy, etc.; X = absent, alk(en/yn)ylene; Y = absent, O, amino, SO0-2, CO; Z = (hetero)cycle; Ua = absent, O, amino, CO, alkyl, carboxy, etc.; Xa = absent, alk(en/yn)ylene; Ya = absent, O, amino, SO0-2, CO; Za = (hetero)cycle; R1-2 together with the carbon atoms to which they are attached, combine to form a 3-8 membered carbocyclic or heterocyclic ring; R3 = H, CHF2, CH2F, CF3, alk(en/yn)ylene, etc.; R4-7 = H, alk(en/yn)yl; n = 0-1] were prepd. For instance, 2-(ethylcarboxy)cyclohexanone was treated with ammonium carbonate and potassium cyanide (EtOHaq, 50°, 24 h) to afford the corresponding hydantoin ester which was hydrolyzed to the carboxylic acid and coupled to 4-[(2-methyl-4-quinolinyl)methoxy]aniline•2HCl (DMSO, PyBOP) to give II which was isolated as the trifluoroacetate. I are useful as inhibitors of matrix metallproteinases (MMP), TNF-α converting enzyme (TACE), aggrecanase, or a combination thereof.

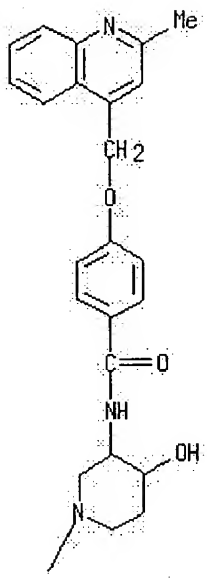
IT **477584-63-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(hydantion derivs. as inhibitors of matrix metalloproteinases)

RN 477584-63-7 HCAPLUS

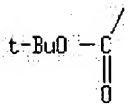
CN 1-Piperidinecarboxylic acid, 4-hydroxy-3-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

h eb c g cg b cg eb

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2             8 S L1
L3           813 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 15:50:21 ON 26 AUG 2004
L4            28 S L3
L5             3 S L4 AND LU, Z?/AU
L6            25 S L4 NOT L5
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L9             0 S L8 AND VOSS, M?/AU
L10            1 S L8 AND XUE, C?/AU

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L11           20 L8 NOT L10

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            732 DUAN, J?/AU
L12           2 L11 AND DUAN, J?/AU

=> d l12, ibib abs fhitstr, 1-2

L12  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
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h eb c g cg b cg eb

Full Text | Citing References

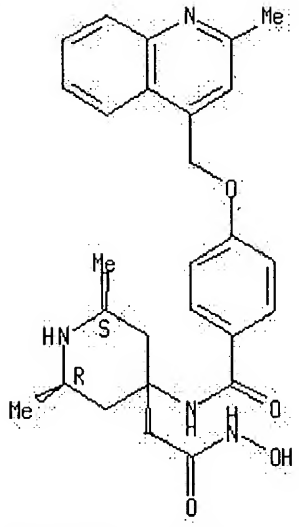
ACCESSION NUMBER: 2004:292661 HCAPLUS
DOCUMENT NUMBER: 141:17257
TITLE: Inhibition of tumor necrosis factor-α-converting enzyme by a selective antagonist protects brain from focal ischemic injury in rats
AUTHOR(S): Wang, Xinkang; Feuerstein, Giora Z.; Xu, Lin; Wang, Hugh; Schumacher, William A.; Ogletree, Martin L.; Taub, Rebecca; **Duan, James J.-W.**; Decicco, Carl P.; Liu, Rui-Qin
CORPORATE SOURCE: Department of Thrombosis Research, Bristol-Myers Squibb Company, Princeton, NJ, 08543-5400, USA
SOURCE: Molecular Pharmacology (2004), 65(4), 890-896
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tumor necrosis factor α (TNFα) is an immunomodulatory and proinflammatory cytokine implicated in neuroinflammation and neuronal damage in response to cerebral ischemia. Tumor necrosis factor-α converting enzyme (TACE or ADAM17) is a key sheddase that releases TNFα from its inactive cell-bound precursor. Using a selective small mol. inhibitor of TACE, DPH-067517, we tested the hypothesis that inhibition of TNFα formation might have a salutary effect in ischemic stroke induced by embolic occlusion of the middle cerebral artery (MCAO). DPH-067517 selectively inhibited TACE enzyme activity in vitro (Ki = 2.8 nM), and effectively suppressed ischemia-induced increase in sol. TNFα in brain tissue after systemic administration. DPH-067517 (3 and 30 mg/kg, i.p. administered 15 min before MCAO) produced 43% (n = 8, p = 0.16) and 58% (n = 8, p < 0.05) redn. in infarct size and 36% (p < 0.05) and 23% (p < 0.05) redn. in neurol. deficits, resp. The salutary effect of DPH-067517 in ischemic brain injury was also obsd. when the first dose was administered 60 min after the onset of ischemia. Inhibition of TACE had no effect on apoptosis measured by levels of active caspase-3 expression and DNA fragmentation. Our data suggest that inhibition of TACE might be a potential therapeutic strategy for neuroprotection after focal ischemic stroke.

IT **362698-30-4**, DPH 067517
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of tumor necrosis factor-α-converting enzyme by a selective antagonist protects brain from focal ischemic injury in rats)

RN 362698-30-4 HCAPLUS
CN 4-Piperidineacetamide, N-hydroxy-2,6-dimethyl-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (2α,4β,6α)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:950052 HCAPLUS
DOCUMENT NUMBER: 140:13040
TITLE: Combined use of TACE inhibitors and COX2 inhibitors as anti-inflammatory agents
INVENTOR(S): **Duan, Jingwu**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2003225054 | A1 | 20031204 | US 2003-453036 | | 20030603 |
| PRIORITY APPLN. INFO.: | | | US 2002-385656P | P | 20020603 |

OTHER SOURCE(S): MARPAT 140:13040

AB This invention relates to a method of treating inflammatory diseases in a mammal comprising administering to the mammal a therapeutically effective amt. of a combination of: (i) at least one TACE inhibitor, (ii) one or more anti-inflammatory agents selected from the group consisting of: selective COX-2 inhibitors, interleukin-1 antagonists, dihydroorotate synthase inhibitors, p38 MAP kinase inhibitors, TNF-α inhibitors, TNF-α sequestration agents, and methotrexate. The invention also relates to compns. and kits contg. the same.

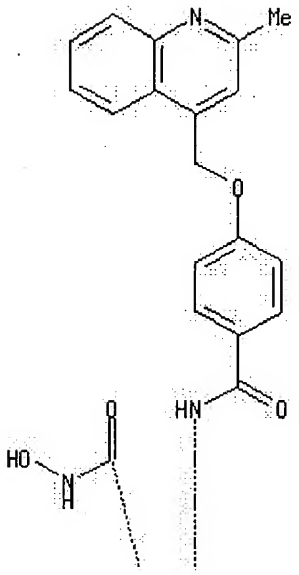
IT **362485-76-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined use of TACE inhibitors and COX2 inhibitors as anti-inflammatory agents)

RN 362485-76-5 HCAPLUS
CN 3-Piperidinecarboxamide, N-hydroxy-1-methyl-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

h eb c g cg b cg eb

PAGE 1-A

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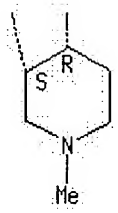


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L2             8 S L1
L3           813 S L1 FULL

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L4            28 S L3
L5             3 S L4 AND LU, Z?/AU
L6            25 S L4 NOT L5
L7             4 S L6 AND MADUSKUIE, T?/AU
L8            21 S L6 NOT L7
L9             0 S L8 AND VOSS, M?/AU
L10            1 S L8 AND XUE, C?/AU
L11           20 S L8 NOT L10
L12            2 S L11 AND DUAN, J?/AU

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            333 OTT, G?/AU
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L15           0 L13 AND CHEN, L?/AU

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           130 DECICCO, C?/AU
L16           0 L13 AND DECICCO, C?/AU

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L13  ANSWER 1 OF 18  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Cited References

ACCESSION NUMBER: 2004:512993 HCAPLUS
DOCUMENT NUMBER: 141:76809
TITLE: Anti-inflammatory coatings for implantable medical devices containing a TACE inhibitor
INVENTOR(S): Dodd, John H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

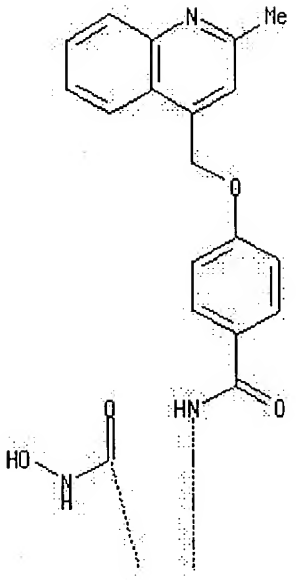
| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2004120977 | A1 | 20040624 | US 2003-732570 | | 20031210 |
| PRIORITY APPLN. INFO.: | | | US 2002-434007P | P | 20021217 |
| | | | US 2003-482273P | P | 20030625 |

AB The present invention relates to implantable surgical medical devices having coatings comprising one or more compds. that inhibit TNF-α converting enzyme (TACE), more particularly, stents having coatings comprising TACE inhibitors. A TACE inhibitor is effective in reducing restenosis.

IT **362485-76-5**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-inflammatory coatings for implantable medical devices contg. TACE inhibitor)
RN 362485-76-5 HCAPLUS
CN 3-Piperidinecarboxamide, N-hydroxy-1-methyl-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

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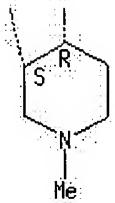


L13 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:331915 HCAPLUS
DOCUMENT NUMBER: 140:357353
TITLE: Preparation of triazolone and triazolethione inhibitors of matrix metalloproteinases and/or TNF-α converting enzyme as anti-inflammatory agents
INVENTOR(S): King, Bryan W.; Sheppeck, James; Gilmore, John L.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004032846 | A2 | 20040422 | WO 2003-US31537 | 20031003 |
| WO 2004032846 | A3 | 20040715 | | |

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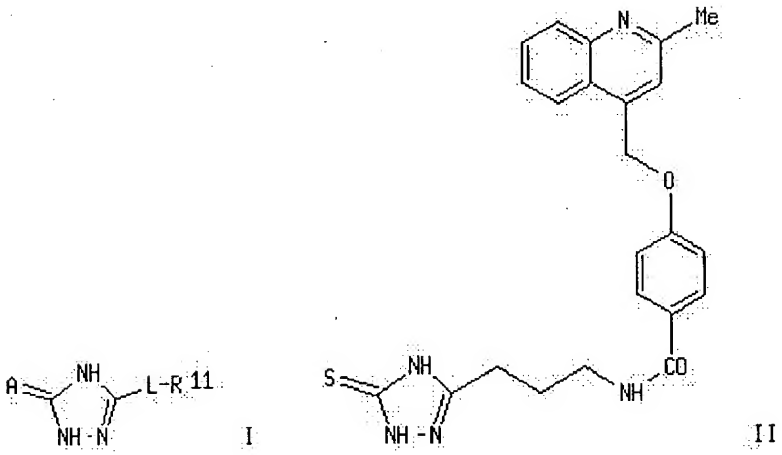
h eb c g cg b cg eb

TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004116491 A1 20040617 US 2003-678331 20031003
PRIORITY APPLN. INFO.: US 2002-416709P P 20021007
OTHER SOURCE(S): MARPAT 140:357353
GI



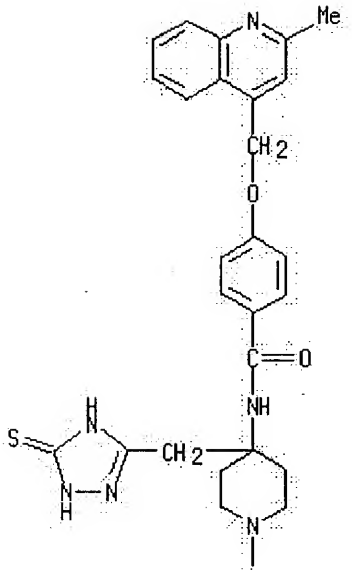

AB The present application describes novel hydantoin derivs. (shown as I; A = O, S; L-R11 represents a very large variety of substituents and is defined in the claims; e.g. II) or pharmaceutically acceptable salt or prodrug forms thereof, which are useful as inhibitors of matrix metalloproteinases (MMP), TNF-α converting enzyme (TACE), aggrecanase, or a combination thereof. Some examples of I exhibit Ki's <10 μM but individual data are not presented. Although the methods of prepn. are not claimed, 37 example prepns. are included. For example, II was prepd. in 4 steps (100, 66, 73 and 82%, resp.) starting with condensation of Et 4-aminobutyrate hydrochloride with 4-(2-methylquinolin-4-ylmethoxy)benzoyl chloride hydrochloride followed by base hydrolysis to the acid, followed by hydrazide formation with thiosemicarbazide followed by cyclization.

IT **681283-94-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of triazolone and triazolethione inhibitors of matrix metalloproteinases and/or TNF-α converting enzyme as anti-inflammatory agents)

RN 681283-94-3 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[(2,5-dihydro-5-thioxo-1H-1,2,4-triazol-3-yl)methyl]-4-[[4-[(2-methyl-4-quinolinyl)methoxy]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

h eb c g cg b cg eb

PAGE 1-A



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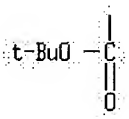

L13 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:291088 HCAPLUS
DOCUMENT NUMBER: 140:321350
TITLE: Preparation of indazolecarboxamides as CDK1, CDK2, and CDK4 inhibitors for treating CDK-related diseases, in particular cancer
INVENTOR(S): D'Orchymont, Hugues; Van Hijfte, Luc; Zimmermann, Andre
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
SOURCE: Fr. Demande, 90 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 2845382 | A1 | 20040409 | FR 2002-12188 | 20021002 |
| WO 2004031158 | A1 | 20040415 | WO 2003-FR2862 | 20030930 |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,

h eb c g cg b cg eb

NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: FR 2002-12188 A 20021002

OTHER SOURCE(S): MARPAT 140:321350

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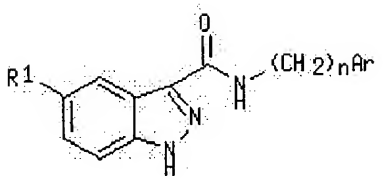


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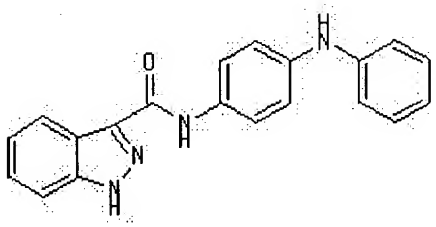


II

AB Title compds. I [R1 = H, halo, NH2, NHR2, NHCOR2, NO2, CN, CH2NH2, CH2NHR2, (un)substituted Ph, heteroaryl; Ar = (un)substituted Ph, heteroaryl; R2 = Ph, heteroaryl, (un)substituted alkyl (substitutent = Ph or heteroaryl); n = 0, 1, 2, or 3; PG = protecting group selected from trimethylsilylethoxymethyl, mesitylenesulfonyl; their free bases, addn. salts with acids, solvates and hydrates; with the exclusion of certain compds.] were prepd. as cyclin-dependent kinase (CDK)-1, CDK2, and CDK4 inhibitors for treating cdk-related diseases, in particular cancer. For instance, reacting indazole-3-carboxylic acid with N-phenyl-1,4-phenylenediamine in the presence of DCC gave 58% II. I displayed IC50 values < 20 μM for the inhibition of CDK2, CDK1, and CDK4 in a test for measuring the enzymic activity of CDK2/Cyclin A, CDK1/Cyclin B, and CDK4/Cyclin D1, resp. I are useful for treating cancers, autoimmune diseases, inflammations, cardiovascular diseases, viral and fungal infections, hematol. diseases, and degenerative diseases of muscular system.

IT **677702-10-2P**, N-(Pyridin-4-yl)-5-[4-methyl-5-(phenoxymethyl)pyridin-3-yl]-1H-indazole-3-carboxamide hydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; prepn. of indazolecarboxamides as cdk1, cdk2, and cdk4 inhibitors)

RN 677702-10-2 HCAPLUS

CN 1H-Indazole-3-carboxamide, 5-[4-methyl-5-(phenoxymethyl)-3-pyridinyl]-N-4-pyridinyl-, monohydrochloride (9CI) (CA INDEX NAME)

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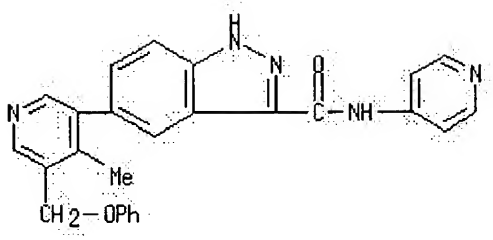


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REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:931365 HCAPLUS
DOCUMENT NUMBER: 140:5078
TITLE: Preparation of dipyridodiazepine non-nucleoside reverse transcriptase inhibitors
INVENTOR(S): Simoneau, Bruno; Landry, Serge; Malenfant, Eric; Naud, Julie; O'meara, Jeffrey; Thavonekham, Bounkham; Yoakim, Christiane
PATENT ASSIGNEE(S): Boehringer Ingelheim International Gmbh, Germany
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003097644 | A2 | 20031127 | WO 2003-CA718 | 20030514 |
| WO 2003097644 | A3 | 20040205 | | |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
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| US 2004006071 | A1 | 20040108 | US 2003-430116 | 20030506 |
| PRIORITY APPLN. INFO.: | | | US 2002-380886P | P 20020516 |

OTHER SOURCE(S): MARPAT 140:5078
GI

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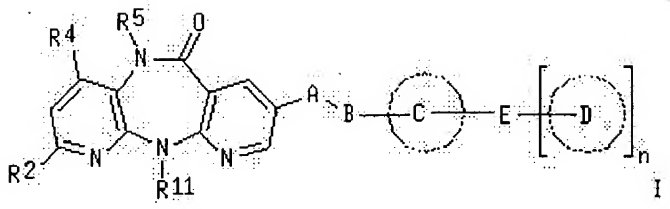

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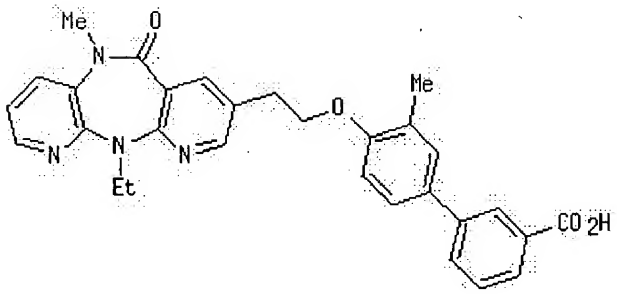

II

AB The title compds. [I; R2 = H, alkyl, halo, haloalkyl, OH, alkoxy, NH(alkyl) or N(alkyl)2; R4 = H, Me; R5 = H, Me; R11 = H, alkyl, cycloalkyl and alkylcycloalkyl; A = alkylene; B = O, S; n = 0-1; when n = 0, Ring C = (un)substituted 6-10 membered aryl, 5-6 membered heterocycle having from 1-4 heteroatoms selected from O, N, and S; E = CONR12R13 (R12, R13 = H, SO2alkyl, alkylCO2H, alkylcycloalkyl), CONHNR14R15 (R14, R15 = H, alkyl optionally substituted by CO2H), NR16COR17 (R16 = H, alkyl optionally substituted with CO2H, arylCO2H; R17 = alkenylCO2H, cycloalkylCO2H, NHalkylCO2H, etc.), NR18SO2alkyl (R18 = H, alkyl), SO2NR19R20 (R19 = H, alkyl; R20 = alkyl optionally substituted with CO2H), SO2R21 (R21 = alkyl); or when n = 1, Ring C is as defined above and E = a single bond or a connecting group; Ring D = (un)substituted 6-10 membered aryl, 5-6 membered heterocycle having from 1-4 heteroatoms selected from O, N, and S] or a salts or a prodrugs thereof, useful as inhibitors of HIV reverse transcriptase, were prepd. Thus, reacting 11-ethyl-5,11-dihydro-8-(2-hydroxyethyl)-5-methyl-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one with Me 4'-hydroxy-3'-methyl-[1,1'-biphenyl]-4-carboxylate (prepn. given) in the presence of DEAD, PPh3 in THF followed by hydrolysis of the resulting ester afforded II which showed IC50 of <10 nM in wild type RT assay. Pharmaceutical compn. for the treatment or prevention of HIV infection, comprising the compd. I is claimed.

IT **627905-95-7P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of dipyridodiazepine non-nucleoside reverse transcriptase inhibitors)

RN 627905-95-7 HCAPLUS

CN Benzamide, 4-[2-(11-ethyl-6,11-dihydro-5-methyl-6-oxo-5H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-8-yl)ethoxy]-3-methyl-N-(1-oxido-4-pyridinyl)-(9CI) (CA INDEX NAME)

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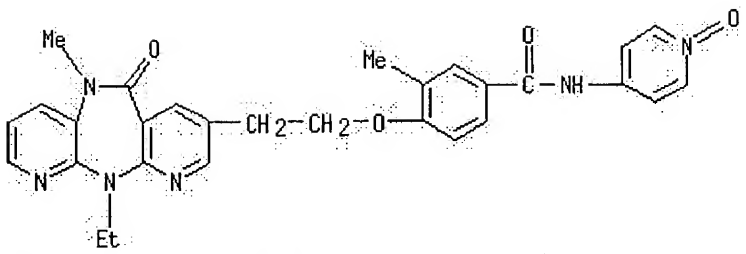

L13 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:532638 HCAPLUS
DOCUMENT NUMBER: 139:101146
TITLE: Preparation of benzyl or heterocyclylmethyl phenyl or heterocyclyl sulfones as β-amyloid protein production/secretion inhibitors
INVENTOR(S): Yasukochi, Takanori; Ito, Masayuki; Kubota, Hideki; Miyauchi, Satoshi; Saito, Masaki
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 540 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003055850 | A1 | 20030710 | WO 2002-JP13792 | 20021227 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-395701 A 20011227
OTHER SOURCE(S): MARPAT 139:101146

AB Novel compds. having various substituents as represented by the following general formula R1(R2)(R3)C-X-R4, salts thereof, and solvates of the same [wherein X = S, SO, SO2; R1 = CR5R6R7, NR8R9, X1R10, X2R11; wherein R5, R6, R7 = halo, cyano, NO2, -Q51-Q52-Q53-Q54; Q51, Q53 = single bond, CO, S(O), SO2, COCO, COC(S), C(S)C(S); Q52 = single bond, O, ON(A51), ON(COA51), N(A51), N(COA51), N(CO2A51), N[CON(A51)(A52)], N(OA51), N(NA51A52), N(A51)N(A52), N(COA51)N(A52), N(A51)-O, N(COA51)-O, S, N:N, C(A51):N, C(A51):N-O, C(A51):N-N(A52), N:C(A51), O-N:C(A51), N(A51)-N:C(A52), C(:NA51)-N(A52); Q54 = A53, OA53, N(A53)(A54), SA53, NA54-OA53, NA55-N(A53)(A54), O-N(A53)(A54); wherein A51, A52, A53 = H, (un)substituted hydrocarbyl or heterocyclyl; R2, R3, R4, R8, R9, R10, R11 = -Q51-Q52-Q53-Q54 defined in R5-R7; X1 = O, S; X2 = SO, SO2; or R1 and R2 or R3 and R4 are combined together to form (un)substituted cyclohydrocarbyl or heterocyclyl] are prepd. These compds. have an effect of inhibiting the prodn./secretion of a β-amyloid protein and are useful for the prevention or treatment of diseases caused by unusual

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prodn./secretion of β-amyloid, in particular Alzheimer's disease or Down's syndrome. Thus, a soln. of 100 mg 2,5-dichloro-4-[(4-chlorophenylthio)-(2,5-difluorophenyl)methyl]pyridine (prepn. given) and 200 μL morpholine in 1.0 mL 1,4-dioxane was stirred at 100° for 2 days to give 4-[5-chloro-4-[(4-chlorophenylthio)-(2,5-difluorophenyl)methyl]pyridin-2-yl]morpholine which (90 mg) was dissolved in 12 mL MeOH, treated with 60 mg ammonium molybdate tetrahydrate [(NH4)6Mo7O24.4H2O] and 6 mL 30% H2O2, and stirred for 8 h to give 83% 4-[5-chloro-4-[(4-chlorophenylsulfonyl)-(2,5-difluorophenyl)methyl]pyridin-2-yl]morpholine (I). I in vitro glioma cell (H4 cell) expressing human β-amyloid protein precursor protein gene (APP751 gene) with EC50 of ≤50 nM.

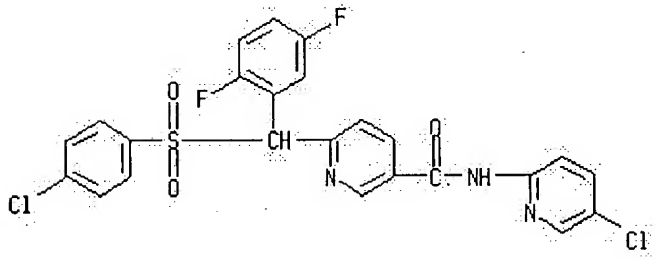
IT **558465-17-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of benzyl or heterocyclylmethyl Ph or heterocyclyl sulfones as β-amyloid protein prodn./secretion inhibitors for treatment or prepn. of Alzheimer's disease or Down's syndrome)

RN 558465-17-1 HCAPLUS

CN 3-Pyridinecarboxamide, 6-[[(4-chlorophenyl)sulfonyl](2,5-difluorophenyl)methyl]-N-(5-chloro-2-pyridinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:5785 HCAPLUS
DOCUMENT NUMBER: 138:73180
TITLE: Preparation of amino-nicotinate derivatives for therapeutic use as glucokinase (GLK) modulators
INVENTOR(S): Hayter, Barry Raymond; Currie, Gordon Stuart; Hargreaves, Rodney Brian; James, Roger; Jones, Clifford David; Mckerrecher, Darren; Allen, Joanne Victoria; Caulkett, Peter William Rodney; Johnstone, Craig; Gaskin, Harold
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003000267 | A1 | 20030103 | WO 2002-GB2873 | 20020624 |

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1404335 A1 20040407 EP 2002-740900 20020624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

BR 2002010711 A 20040720 BR 2002-10711 20020624

PRIORITY APPLN. INFO.: SE 2001-2300 A 20010626
WO 2002-GB2873 W 20020624

OTHER SOURCE(S): MARPAT 138:73180

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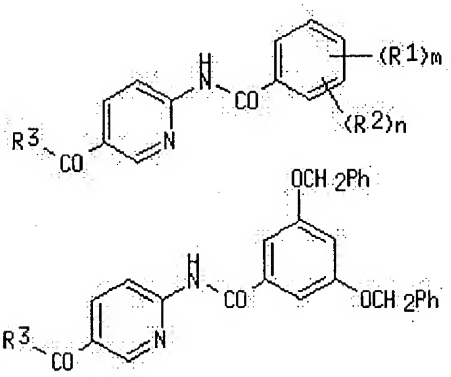


AB Aminonicotinates, such as I [R1 = H, OH, (CH2)1-4OH, NO2, NH2, haloalkyl, haloalkyloxy, alkyl, alkenyl, alkylamino, etc.; R2 = X-Y; X = linking group, such as O, CO, amino, Z-O-Z, etc; Z = alkylene, alkenylene, etc.; R3 = OH, alkoxy, alkylamino, etc.; m = 0-2; n = 0-4; m + n > 0], were prepd. for pharmaceutical use in the treatment of diseases or conditions mediated through glucokinase (GLK), such as type 2 diabetes. Thus, nicotinic acid deriv. II (R3 = OH) was prepd. by treatment of 3,5-dibenzyloxybenzoic acid with oxalyl chloride in CH2Cl2 and DMF followed by addn. of Me 6-aminonicotinate to the reaction mixt. form ester II (R3 = OMe) in 57% yield and subsequent hydrolysis of the ester using LiOH in THF/H2O to give the desired acid in 17% yield. The prepd. compds. were assayed for their effect on GLK activity, and pharmaceutical compns. of the prepd. compds. were presented.

IT **480463-03-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino nicotinate derivs. for therapeutic use as glucokinase (GLK) modulators)

RN 480463-03-4 HCAPLUS

CN 3-Pyridinecarboxylic acid, 6-[[3-(1-methylethoxy)-5-(2-pyridinylmethoxy)benzoyl]amino]- (9CI) (CA INDEX NAME)

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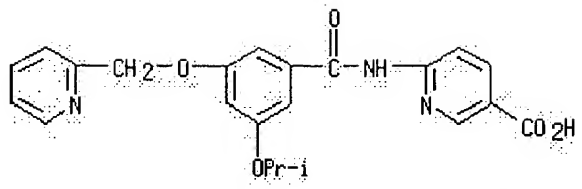

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:754333 HCAPLUS
DOCUMENT NUMBER: 137:279214
TITLE: Preparation of benzoic acid derivatives as nuclear factor κB inhibitors
INVENTOR(S): Suzuki, Kenji; Nunokawa, Youichi; Ogou, Naohisa
PATENT ASSIGNEE(S): Suntory Limited, Japan; Suntory Biomedical Research Limited
SOURCE: PCT Int. Appl., 243 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2002076918 | A1 | 20021003 | WO 2002-JP3017 | | 20020327 |
| WO 2002076918 | C1 | 20021031 | | | |
| W: BR, CA, CN, HU, JP, KR, US | | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | | |
| BR 2002004678 | A | 20030429 | BR 2002-4678 | | 20020327 |
| EP 1314712 | A1 | 20030528 | EP 2002-708696 | | 20020327 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | | | |
| US 2004122244 | A1 | 20040624 | US 2002-296810 | | 20021127 |
| PRIORITY APPLN. INFO.: | | | JP 2001-91003 | A | 20010327 |
| | | | WO 2002-JP3017 | W | 20020327 |

OTHER SOURCE(S): MARPAT 137:279214
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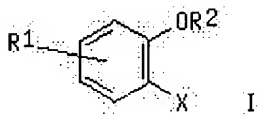

I

AB The title compds. I [R1 = (1,4-benzoquinon-2-yl)methyl (with substituents selected from H, alkyl, etc.) (generic structure given), etc.; R2 = H, (un)substituted alkyl, etc.; X = carboxyl (which may esterified or amidated)] are prepd. In an in vitro test for nuclear factor κB inhibiting activity, N-[5-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-yl)methyl-2-hydroxybenzoyl]-4-aminobenzoic acid Et ester showed IC50 value of 3 μg/mL.

IT **464215-26-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

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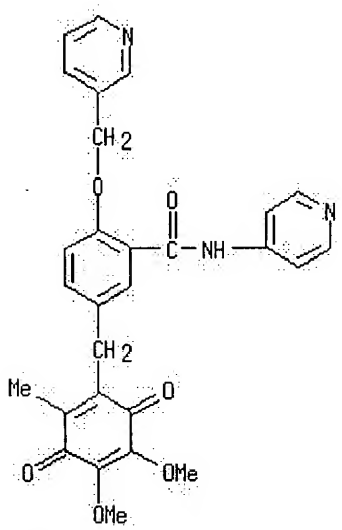
(Uses)
(prepn. of benzoic acid derivs. as nuclear factor κB inhibitors)
RN 464215-26-7 HCAPLUS
CN Benzamide, 5-[(4,5-dimethoxy-2-methyl-3,6-dioxo-1,4-cyclohexadien-1-yl)methyl]-N-4-pyridinyl-2-(3-pyridinylmethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:591913 HCAPLUS
DOCUMENT NUMBER: 137:150215
TITLE: Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents
INVENTOR(S): Hatayama, Satoshi; Hayashi, Kyoko; Honma, Mitsuki; Takahashi, Ikuko
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 194 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 2002220338 | A2 | 20020809 | JP 2001-18755 | 20010126 |
| PRIORITY APPLN. INFO.: | | | JP 2001-18755 | 20010126 |

OTHER SOURCE(S): MARPAT 137:150215
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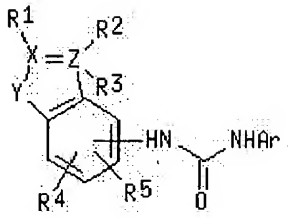



I

AB This invention relates to the general structures (I; Ar = N-contg. hetero arom. ring, X, Z = C, etc.; Y = CO, etc.; R1-R5 = H, etc.) and their salts as Cdk4 and/or Cdk6 inhibitors. I have antiproliferative effects on cancer cells and are potential antitumor agents. Formulation examples of I capsules, tablets, and injections were given.

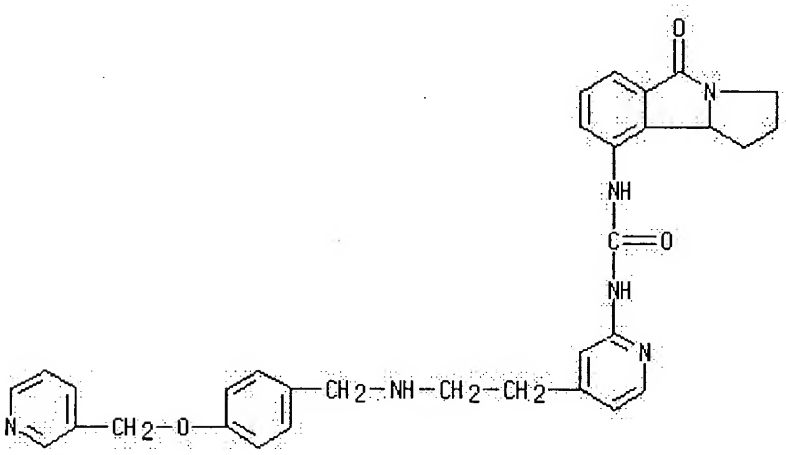
IT **322686-55-5**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents)

RN 322686-55-5 HCAPLUS

CN Urea, N-[4-[2-[[[4-(3-pyridinylmethoxy)phenyl]methyl]amino]ethyl]-2-pyridinyl]-N'-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)- (9CI) (CA INDEX NAME)




L13 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | CHIP | References

| | |
|---|---|
| ACCESSION NUMBER: | 2001:886851 HCAPLUS |
| DOCUMENT NUMBER: | 136:20023 |
| TITLE: | Preparation of pyridine-substituted benzanilides as potassium channel openers |
| INVENTOR(S): | McNaughton-Smith, Grant; Fritch, Paul Christopher; Amato, George Salvatore |
| PATENT ASSIGNEE(S): | USA |
| SOURCE: | U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U.S. Ser. No. 632,576.<br>CODEN: USXXCO |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 3 |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

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09/939230

| | | | | |
|---|---|---|---|---|
| US 2001049444 | A1 | 20011206 | US 2001-776791 | 20010202 |
| US 6495550 | B2 | 20021217 | | |
| US 6326385 | B1 | 20011204 | US 2000-631747 | 20000804 |
| US 6372767 | B1 | 20020416 | US 2000-632576 | 20000804 |
| US 2002013349 | A1 | 20020131 | US 2001-939230 | 20010824 |
| US 2002091122 | A1 | 20020711 | US 2001-4122 | 20011101 |
| US 6737422 | B2 | 20040518 | | |
| US 2002052393 | A1 | 20020502 | US 2001-2800 | 20011102 |
| US 6605725 | B2 | 20030812 | | |
| WO 2002062295 | A2 | 20020815 | WO 2002-US3061 | 20020201 |
| WO 2002062295 | A3 | 20030703 | | |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|
| EP 1363884 | A2 | 20031126 | EP 2002-704333 | 20020201 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1999-147221P | P | 19990804 |
| US 2000-632576 | A2 | 20000804 |
| US 1999-158712P | P | 19991008 |
| US 1999-165847P | P | 19991116 |
| US 2000-631747 | A | 20000804 |
| US 2001-776791 | A | 20010202 |
| WO 2002-US3061 | W | 20020201 |

OTHER SOURCE(S): MARPAT 136:20023

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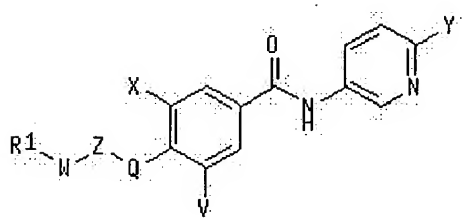


I

AB The title compds. [I; Y = H, Me, OMe, OCF3, halo; V, X = H, halo, alkyl, etc.; R1 = alkyl, heteroalkyl, aryl, etc.; Q, W = C≡C, (un)substituted CH:CH, alkylene; Z = O, CO, (un)substituted NH, etc.] which are voltage-dependent potassium channel openers, and are useful for the treatment of central and peripheral nervous system disorders, were prepd. General procedures for prepg. compds. I such as 3,4-dichloro-N-(pyridin-3-yl)benzamide were given. The activity of compds. I, assayed according to a KCNQ2 screening protocol, ranged from about 30% to greater than about 70% efflux.

IT **378241-17-9P**

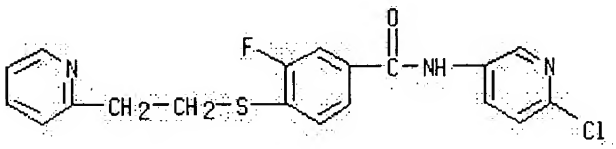
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of benzanilides as potassium channel openers)

RN 378241-17-9 HCAPLUS

h eb c g cg b cg eb

CN Benzamide, N-(6-chloro-3-pyridinyl)-3-fluoro-4-[[2-(2-pyridinyl)ethyl]thio]- (9CI) (CA INDEX NAME)



L13 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:78363 HCAPLUS
DOCUMENT NUMBER: 134:147614
TITLE: Preparation of N,N'-biarylurea derivatives as inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6)
INVENTOR(S): Hayama, Takashi; Hayashi, Kyoko; Honma, Mitsutaka; Takahashi, Ikuko
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 460 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001007411 | A1 | 20010201 | WO 2000-JP4991 | 20000726 |
| W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| JP 2001106673 | A2 | 20010417 | JP 2000-274175 | 20000726 |
| EP 1199306 | A1 | 20020424 | EP 2000-949909 | 20000726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |

| PRIORITY APPLN. INFO.: | | |
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| JP 1999-211384 | A | 19990726 |
| WO 2000-JP4991 | W | 20000726 |

OTHER SOURCE(S): MARPAT 134:147614
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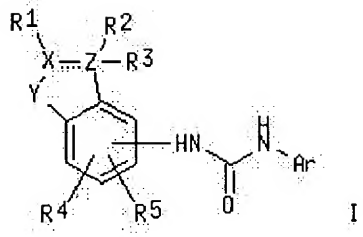

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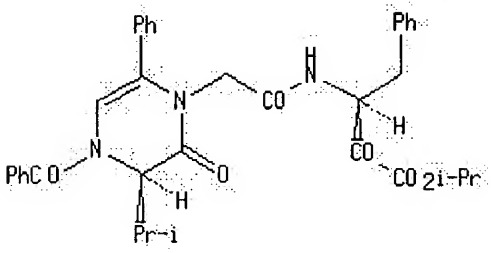


II

AB N-(hetero)aryl-N'-heterocyclylurea derivs. represented by general formula (I) [wherein Ar represents a nitrogenous heterocyclic arom. group such as (un)substituted pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, pyrrolyl, imidazolyl, indolyl, isoindolyl, quinolyl, isoquinolyl, benzothiazolyl, or benzoxazolyl; X and Z each represents C or N or together with R1 or R2 and/or R3 represent CH or N; Y represents CO, SO, or SO2; R1 represents hydrogen, (un)substituted lower alkyl, Y3-W2-Y4-R5, etc.; wherein R5 = H, (un)substituted lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, aryl, imidazolyl, isoxazolyl, isoquinolyl, isoindolyl, indazolyl, indolyl, indolidinyl, isothiazolyl, ethylenedioxyphenyl, oxazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrazolyl, quinoxalinyl, quinolyl, etc.; W2 = ingle bond, O, S, SO, SO2, N-(un)substituted NH, SO2NH, NHSO2NH, NHSO2, CONH, NHCO, NHCONH, NHCO2, etc.; Y3, Y4 = single bond, linear or branched lower alkylene; R2 and R3 each represents hydrogen, lower alkyl or alkoxy, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above), or one of R2 and R3 together with R1 and X forms cyclohexane, cyclopentane, piperidine, 3,4,5,6-tetrahydro-1,3-oxazine, tetrahydrothiopyran, pyrrolidine, tetrahydrothiofuran, oxazolidine ring, etc.; R4 and R5 represent H, halo, OH, amino, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above)] or salts thereof are prepd. The compds. (e.g. II) have a remarkable proliferation-inhibitory effect on tumor cells. A Cdk4 and/or Cdk6 inhibitor for use in the therapy of malignant tumor can hence be provided. II showed IC50 of 0.061 and 0.019 μM against cyclin-D1-Cdk4 and cyclin-D2-Cdk4, resp., vs. 0.36 and 0.056 μM, resp., for (±)-flavopiridol, and inhibited the proliferation of HCT116 and MKN-1 cells with IC50 of 0.013 and 0.10 μM, resp., vs. 0.15 and 0.87 μM, resp., for (±)-flavopiridol. Pharmaceutical formulations contg. I were prepd.

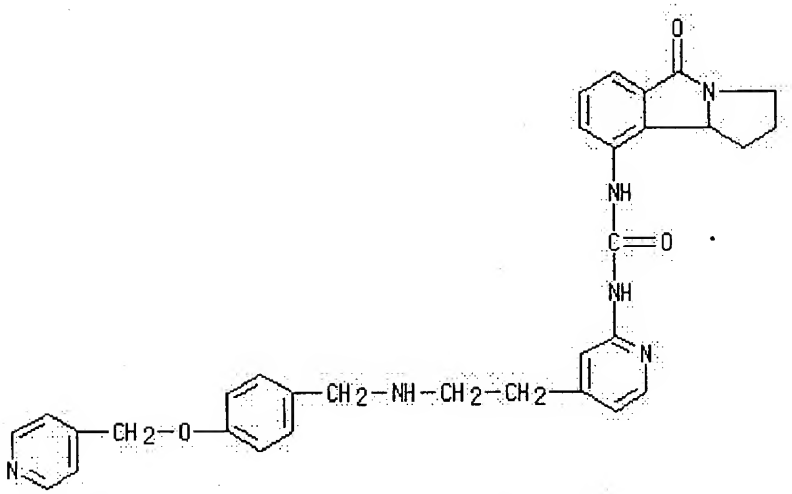
IT **322686-59-9P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(hetero)aryl-N'-heterocyclylurea derivs. as in inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6) and antitumor agents)

RN 322686-59-9 HCAPLUS

CN Urea, N-[4-[2-[[[4-(4-pyridinylmethoxy)phenyl]methyl]amino]ethyl]-2-pyridinyl]-N'-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)-(9CI) (CA INDEX NAME)

h eb c g cg b cg eb



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Other References

ACCESSION NUMBER: 1999:566030 HCAPLUS
DOCUMENT NUMBER: 131:170353
TITLE: Method for preparation of pyridone urea derivatives from amino or carbamoylpyridone derivatives
INVENTOR(S): Muraoka, Masami; Morishita, Koji; Aida, Nagisa; Tanaka, Masashi; Yuri, Masatoshi; Ohashi, Naohito
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9943659 | A1 | 19990902 | WO 1999-JP718 | 19990217 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2321237 | AA | 19990902 | CA 1999-2321237 | 19990217 |
| AU 9925473 | A1 | 19990915 | AU 1999-25473 | 19990217 |
| EP 1086948 | A1 | 20010328 | EP 1999-905228 | 19990217 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI | | | | |
| US 6300500 | B1 | 20011009 | US 2000-623030 | 20000825 |
| US 2001051732 | A1 | 20011213 | US 2001-853953 | 20010514 |
| US 6452008 | B2 | 20020917 | | |

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| JP 1998-62346 | A | 19980225 |
| JP 1998-92567 | A | 19980319 |
| WO 1999-JP718 | W | 19990217 |
| US 2000-623030 | A3 | 20000825 |

OTHER SOURCE(S): CASREACT 131:170353; MARPAT 131:170353
GI

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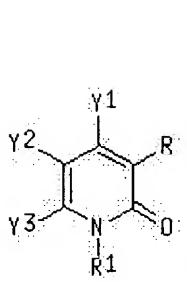
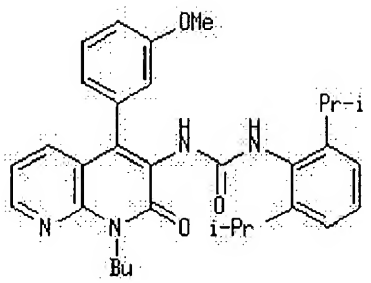



I




II

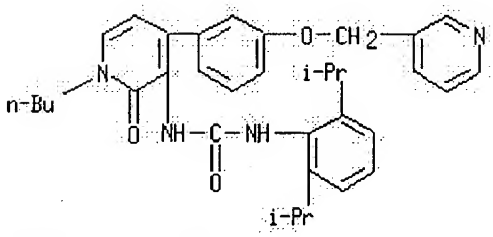
AB A process for producing a pyridone deriv. represented by general formula [I; R = NHCONH-L; R1 = H, (un)substituted alkyl, alkenyl, alkynyl, or cycloalkyl; Y1 = H, (un)substituted alkyl, cycloalkyl, or arom. group; Y2, Y3 = H, halo, OH, cyano, CF3, NO2, NH2 mono- or dialkylamino, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, (un)substituted alkyl, cycloalkyl, or arom. group; or Y2 and Y3 are linked together to form an (un)substituted pyridine] is characterized by reacting (oxidizing) a carbamoylpyridone represented by general formula I (R = CONH2) with a hypochlorite or hypobromite or with lead tetraacetate to give isocyanatopyridone represented by general formula I(R = isocyanato) and reacting this compd. with an amine represented by general formula L-NH2. The process is preferable, esp. from the standpoint of safety. The N-(2-oxo-1,2-dihydropyridyl)urea derivs. possess acyl-CoA:cholesterol acyltransferase (ACAT) inhibitory-activity and are useful for the treatment of hyperlipidemia and arteriosclerosis (no data). Thus, 14.5 g lead tetraacetate was added to a suspension of 10.0 g 1-butyl-3-carbamoyl-4-(3-methoxyphenyl)-1,2-dihydro-2-oxo-1,8-naphthyridine in 100 mL DMF and stirred at room temp. for 0.5 h, followed by adding 5.3 g 2,6-diisopropylaniline at room temp., and the resulting mixt. was stirred at 40-50° for 1.5 h to give 68% N-(1,2-dihydro-2-oxo-1,8-naphthyridin-3-yl)-N'-phenylurea (II).

IT 239098-59-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(dihydrooxopyridyl)urea derivs. from amino or carbamoylpyridone derivs.)

RN 239098-59-0 HCAPLUS

CN Urea, N-[2,6-bis(1-methylethyl)phenyl]-N'-[1-butyl-1,2-dihydro-2-oxo-4-[3-(3-pyridinylmethoxy)phenyl]-3-pyridinyl]- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:464280 HCAPLUS

DOCUMENT NUMBER: 131:116153

h eb c g cg b cg eb

TITLE: Preparation of N-(phenylcyclopropyl)-N'-pyridylurea derivatives as antivirals and as HIV reverse transcriptase inhibitors

INVENTOR(S): Sahlberg, Christer; Noreen, Rolf; Hogberg, Marita; Engelhardt, Per

PATENT ASSIGNEE(S): Medivir AB, Swed.

SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

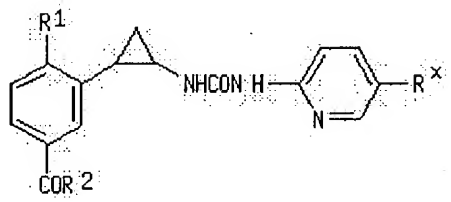
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9936406 | A1 | 19990722 | WO 1999-SE53 | 19990115 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| ZA 9900292 | A | 19990715 | ZA 1999-292 | 19990115 |
| CA 2318694 | AA | 19990722 | CA 1999-2318694 | 19990115 |
| AU 9924450 | A1 | 19990802 | AU 1999-24450 | 19990115 |
| AU 739766 | B2 | 20011018 | | |
| EP 1054867 | A1 | 20001129 | EP 1999-903983 | 19990115 |
| EP 1054867 | B1 | 20040414 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200002058 | T2 | 20010521 | TR 2000-200002058 | 19990115 |
| BR 9906933 | A | 20011127 | BR 1999-6933 | 19990115 |
| TW 470645 | B | 20020101 | TW 1999-88100605 | 19990115 |
| JP 2002509137 | T2 | 20020326 | JP 2000-540122 | 19990115 |
| NZ 505543 | A | 20020927 | NZ 1999-505543 | 19990115 |
| AT 264305 | E | 20040415 | AT 1999-903983 | 19990115 |
| US 6486183 | B1 | 20021126 | US 2000-600309 | 20001113 |
| US 2003119881 | A1 | 20030626 | US 2002-243118 | 20020912 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| SE 1998-113 | A | 19980116 |
| SE 1998-116 | A | 19980116 |
| WO 1999-SE53 | W | 19990115 |
| US 2000-600309 | A3 | 20001113 |

OTHER SOURCE(S): MARPAT 131:116153

GI



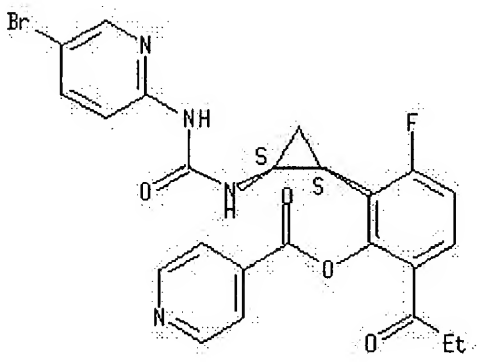

I

AB The title compds. I (Rx = cyano, Br; R1 = halo; R2 = C1-C3 alkyl), antiretrovirals with HIV reverse transcriptase inhibiting activity, were prepd. E.g., (1S,2S)-N-[cis-2-(6-fluoro-2-hydroxy-3-propionylphenyl)cyclopropyl]-N'-(5-cyanopyrid-2-yl)urea was prepd.

h eb c g cg b cg eb

IT 231957-60-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(phenylcyclopropyl)-N'-pyridylurea derivs. as antivirals and as HIV reverse transcriptase inhibitors)
RN 231957-60-1 HCAPLUS
CN 4-Pyridinecarboxylic acid, 2-[(1S,2S)-2-[[[(5-bromo-2-pyridinyl)amino]carbonyl]amino]cyclopropyl]-3-fluoro-6-(1-oxopropyl)phenyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | More References

ACCESSION NUMBER: 1997:218623 HCAPLUS
DOCUMENT NUMBER: 126:212048
TITLE: Substituted aromatic compounds and their pharmaceutical use as inhibitors of TNF and PDE IV.
INVENTOR(S): Aldous, David John; Smith, Graham Frank; Astles, Peter Charles; Pickett, Stephen Dennis; McLay, Iain McFarlane; Stuttle, Keith Alfred James; Ratcliffe, Andrew James; et al.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Limited, UK
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9703967 | A1 | 19970206 | WO 1996-GB1746 | 19960722 |

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM

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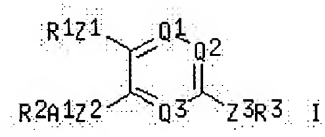
| | | | | | |
|---|---|---|---|---|---|
| AU 9665268 | A1 | 19970218 | AU 1996-65268 | | 19960722 |
| PRIORITY APPLN. INFO.: | | | GB 1995-15058 | A | 19950722 |
| | | | GB 1995-15729 | A | 19950801 |
| | | | GB 1996-4531 | A | 19960302 |
| | | | US 1996-14212P | P | 19960327 |
| | | | WO 1996-GB1746 | W | 19960722 |

OTHER SOURCE(S): MARPAT 126:212048

GI

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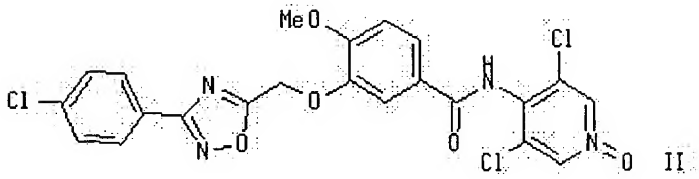


II

AB The invention describes compds. I [wherein R1 = (un)substituted alkyl, or when Z1 = bond, R1 may also = H; R2 = (un)substituted aryl, partially satd. bicycloaryl, heteroaryl, or RaRbN; R3 = (un)substituted aryl or heteroaryl; A1 = bond, (un)substituted C1-6 alkylene or C2-6 alk(en/yn)ylene optionally interrupted by O, S, phenylene, imino, alkylimino, SO, or SO2; Z1, Z2 = O, S or bond; Z3 = C≡C, CH2CZ, CZCH2, CZCZ, CH2NH, CH2O, CH2S, CH2SO, CH2SO2, CF2O, CZNH, NHCH2, OCH2, SCH2, SOCH2, SO2CH2, OCF2, OCZ, NHCZ, N:N, NHSO2, SO2NH, CZCZNH, NHCOO, OCONH, C(:NORc)CH2, C(F):N, CH(F)CH2, or NHCONH; Z = O or S; Ra, Rb = alkyl or arylalkyl; or NRaRb = 4- to 6-membered cyclic amine optionally contg. addnl. O, S, NH, or NRc or substituted with oxo; Rc = alkyl or arylalkyl; Q1, Q2, Q3 = CH, CX1, or N; and X1 = halo] and their N-oxides, prodrugs, pharmaceutically acceptable salts, and solvates (e.g. hydrates). The invention also describes processes for prepg. I, pharmaceutical compns. comprising I, and their use in therapy as inhibitors of TNF and type IV cAMP phosphodiesterase (PDE) (no data). For example, 5-[[(3,5-dichloropyridin-4-yl)imino]fluoromethyl]-2-methoxyphenol (prepn. given) was etherified with 3-(4-chlorophenyl)-5-(hydroxymethyl)-1,2,4-oxadiazole using the Mitsunobu reaction, followed by conversion of the imidoyl fluoride function to an amide using KOSiMe3, and N-oxidn. using m-ClC6H4C(O)OOH, to give title compd. II.

IT **187968-96-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of substituted arom. compds. as inhibitors of TNF and PDE IV)

RN 187968-96-3 HCAPLUS

CN Benzamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy-3-(2-pyridinylmethoxy)- (9CI) (CA INDEX NAME)

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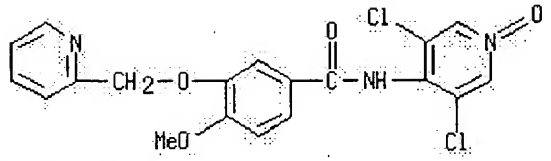

L13 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:337928 HCAPLUS
DOCUMENT NUMBER: 125:33487
TITLE: Iminoxycarboxylates and derivatives as inhibitors of leukotriene biosynthesis
INVENTOR(S): Brooks, Dee W.; Bhatia, Pramila; Kolasa, Teodozyj; Stewart, Andrew O.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9602507 | A1 | 19960201 | WO 1995-US8367 | 19950628 |
| W: AU, CA, JP, KR, MX | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5512581 | A | 19960430 | US 1995-432491 | 19950501 |
| CA 2191975 | AA | 19960201 | CA 1995-2191975 | 19950628 |
| AU 9530023 | A1 | 19960216 | AU 1995-30023 | 19950628 |
| EP 772594 | A1 | 19970514 | EP 1995-926167 | 19950628 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| JP 2001518050 | T2 | 20011009 | JP 1996-505058 | 19950628 |
| PRIORITY APPLN. INFO.: | | | US 1994-276148 A | 19940718 |
| | | | WO 1995-US8367 W | 19950628 |

OTHER SOURCE(S): MARPAT 125:33487
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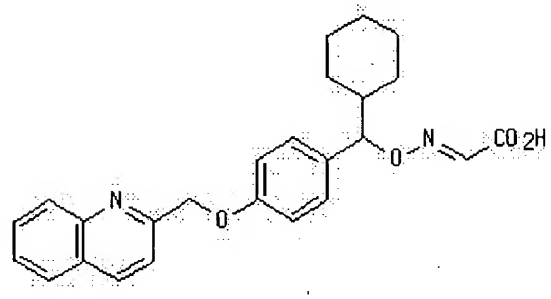

I

AB The title compds. WXYCH(R1)ON:C(R2)ACOM [W = (un)substituted aryl or heteroaryl; X = bond, CH2, alkylene, alkenylene, alkynylene, alkenyloxy; Q = bond, O, S, (un)substituted amino, etc.; Y = (un)substituted Ph, biphenyl, naphthyl, tetrahydronaphthyl, indolyl, pyridyl, benzo[b]thienyl, thienyl, thiazolyl, thiazolylphenyl; R1 = alkyl, cycloalkyl, alkoxyalkyl, aryl or arylalkyl, heteroaryl or heteroarylalkyl; R2 = H, alkyl, hydroxyalkyl; A = bond, alkylene, alkenylene, alkynylene, cycloalkylene, phenylene, pyridylene, thienylene, furylene; M = pharmaceutically

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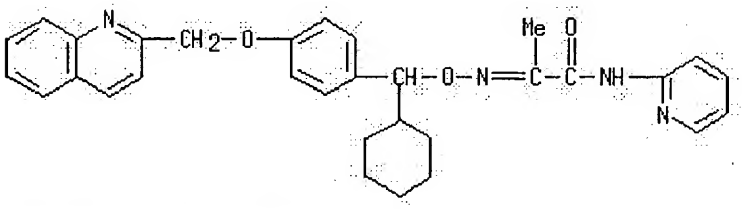
acceptable and metabolically cleavable group, 3-, or 4-pyridyl, 4- or 5-thiazolyl, etc.], which inhibit leukotriene biosynthesis and are useful in the treatment of inflammatory disease states, are prepd. Thus, quinoline deriv. I, prepd. in 5 steps from 4-hydroxybenzaldehyde, demonstrated a IC50 of 0.021 μM against 5-lipoxygenase formation in LTB4-stimulated human polymorphonuclear leukocytes.

IT **177276-04-9P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(iminoxycarboxylates and derivs. as inhibitors of leukotriene biosynthesis)

RN 177276-04-9 HCAPLUS

CN Propanamide, 2-[[cyclohexyl[4-(2-quinolinylmethoxy)phenyl]methoxy]imino]-N-2-pyridinyl- (9CI) (CA INDEX NAME)



L13 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

| | |
|---|---|
| ACCESSION NUMBER: | 1994:621558 HCAPLUS |
| DOCUMENT NUMBER: | 121:221558 |
| TITLE: | Synthesis of new potent leukotriene B4 antagonists and their biological properties. 2. |
| AUTHOR(S): | Kawakami, Hajime; Ohmi, Naoko; Nagata, Hideo |
| CORPORATE SOURCE: | Sumitomo Pharmaceuticals Research Center, Osaka, 554, Japan |
| SOURCE: | Bioorganic & Medicinal Chemistry Letters (1994), 4(12), 1461-6<br>CODEN: BMCLE8; ISSN: 0960-894X |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | English |

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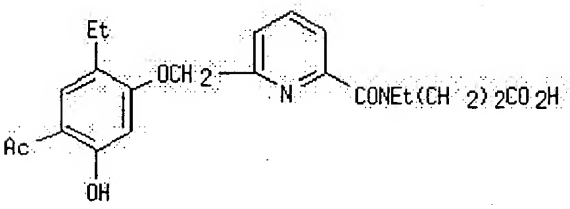

I

AB The synthesis of new leukotriene B4 antagonists and their biol. properties are described. SM-15178 (I) has potent effects against human neutrophil chemotaxis, and is orally effective against LTB4-induced bronchoconstriction in the guinea pig.

IT **146460-42-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

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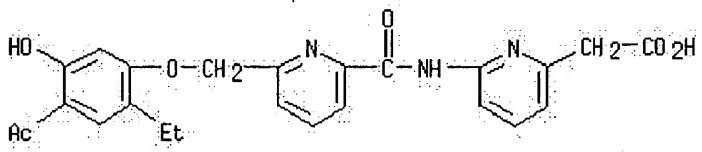
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and pharmacol. of leukotriene B4 antagonists)
RN 146460-42-6 HCAPLUS
CN 2-Pyridineacetic acid, 6-[[[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]-2-pyridinyl]carbonyl]amino]- (9CI) (CA INDEX NAME)



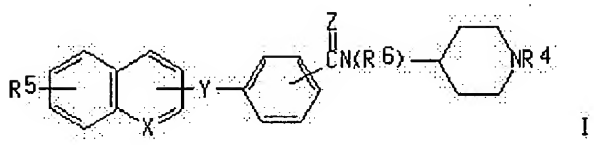

L13 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | More References

ACCESSION NUMBER: 1993:509007 HCAPLUS
DOCUMENT NUMBER: 119:109007
TITLE: Substituted quinolinyl- and naphthalenylbenzamides or benzylamines and related compounds useful as analgesics
INVENTOR(S): Musser, John H.; Molinari, Albert J.; Mobilio, Dominick
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5212182 | A | 19930518 | US 1990-592160 | 19901003 |

PRIORITY APPLN. INFO.: US 1990-592160 19901003
OTHER SOURCE(S): MARPAT 119:109007
GI




I

AB The title compds. are I [X = N, NO, CR1; Y = C(R1)(R2)O, OC(R1)(R2), C(R1)(R2)N(R3), N(R3)C(R1)(R2), C(R1):C(R2) (R1-R3 = H, C1-10 alkyl); Z = O, (R1)(R2); R4 = R1, benzyl, Ph, etc.; R5 = R1, C1-10 alkoxy, halo, trihalomethyl, NO2, etc.; R6 = R1 or C(O)(R7) (with proviso that Z is not O) (R7 = R1, Ph, C1-10 perfluoroalkyl, phenylalkyl with 1-10 C in alkyl group)] and pharmaceutically acceptable acid addn. salts thereof. I are used for treatment of bradykinin-mediated pain. Prepn. of a variety of I is described, and the prepd. compds. were tested in a bradykinin receptor assay and for inhibition of bradykinin-induced writhing in mice.
IT **149326-02-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for analgesic)
RN 149326-02-3 HCAPLUS
CN Benzamide, N-[1-(phenylmethyl)-4-piperidinyl]-4-(4-quinolinylmethoxy)-

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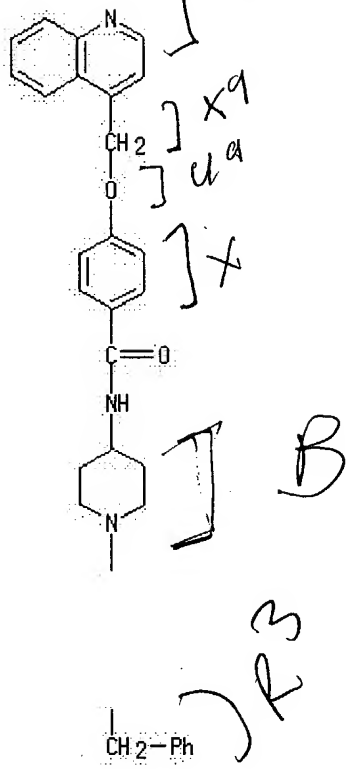
(9CI) (CA INDEX NAME)




L13 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | CAPLUS References

ACCESSION NUMBER: 1993:428148 HCAPLUS
DOCUMENT NUMBER: 119:28148
TITLE: Preparation of N-heterocyclyl-2-[4-(2-quinolylmethoxy)phenyl]acetamides as lipoxygenase inhibitors
INVENTOR(S): Raddatz, Siegfried; Mohrs, Klaus Helmut; Matzke, Michael; Fruchtmann, Romanis; Hatzelmann, Armin; Kohlsdorfer, Christian; Mueller-Peddinghaus, Reiner; Theisen-Popp, Pia
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 530639 | A1 | 19930310 | EP 1992-114428 | 19920825 |
| EP 530639 | B1 | 19940817 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| DE 4129742 | A1 | 19930311 | DE 1991-4129742 | 19910906 |
| NO 9203181 | A | 19930308 | NO 1992-3181 | 19920814 |
| ES 2057953 | T3 | 19941016 | ES 1992-114428 | 19920825 |
| US 5266578 | A | 19931130 | US 1992-936180 | 19920826 |

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| | | | | |
|---|---|---|---|---|
| JP 05194403 | A2 | 19930803 | JP 1992-253582 | 19920831 |
| AU 9222054 | A1 | 19930311 | AU 1992-22054 | 19920901 |
| AU 649351 | B2 | 19940519 | | |
| CA 2077465 | AA | 19930307 | CA 1992-2077465 | 19920903 |
| ZA 9206706 | A | 19930308 | ZA 1992-6706 | 19920904 |
| HU 65660 | A2 | 19940728 | HU 1992-2850 | 19920904 |
| CN 1070190 | A | 19930324 | CN 1992-110346 | 19920905 |

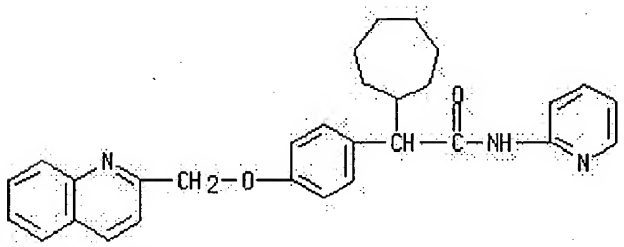
PRIORITY APPLN. INFO.: DE 1991-4129742 19910906
OTHER SOURCE(S): MARPAT 119:28148

AB RCH2OZCHR1CONR2R3 [R = (substituted) 2-quinolyl; R1 = (cyclo)alkyl, aralkyl, etc.; R2 = H, alkyl; R3 = (substituted) heterocyclyl; Z = phenylenediyl] were prepd. Thus, 4-(RCH2O)C6H4CHR1COR4 (R = 2-quinolyl, R1 = cycloheptyl) (I; R4 = OH) was condensed with 2-aminopyridine to give I (R4 = 2-pyridylamino) which had IC50 of 2.6 7-10 ı µM against 5-lipoxygenase in vitro.

IT **148256-28-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as lipoxygenase inhibitor)

RN 148256-28-4 HCAPLUS

CN Cycloheptaneacetamide, N-2-pyridinyl-α-[4-(2-quinolinylmethoxy)phenyl]- (9CI) (CA INDEX NAME)




L13 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Cited References

ACCESSION NUMBER: 1993:169102 HCAPLUS
DOCUMENT NUMBER: 118:169102
TITLE: Preparation of phenoxymethyl(carbamoyl)arenes as leukotriene B4 antagonists
INVENTOR(S): Nagata, Hideo; Kawakami, Hajime
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 147 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 516069 | A1 | 19921202 | EP 1992-108916 | 19920527 |
| EP 516069 | B1 | 19960424 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, PT, SE | | | | |
| CA 2069667 | AA | 19921201 | CA 1992-2069667 | 19920527 |
| AU 9217193 | A1 | 19930311 | AU 1992-17193 | 19920527 |
| AU 643140 | B2 | 19931104 | | |
| AT 137223 | E | 19960515 | AT 1992-108916 | 19920527 |

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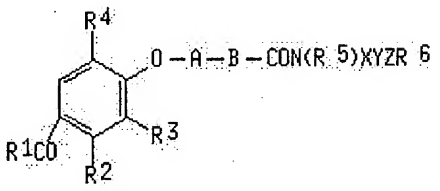
| | | | | |
|---|---|---|---|---|
| ES 2086579 | T3 | 19960701 | ES 1992-108916 | 19920527 |
| JP 05239004 | A2 | 19930917 | JP 1992-164065 | 19920528 |
| US 5225422 | A | 19930706 | US 1992-891256 | 19920601 |
| PRIORITY APPLN. INFO.: | | | JP 1991-157725 | 19910531 |

OTHER SOURCE(S): MARPAT 118:169102
GI

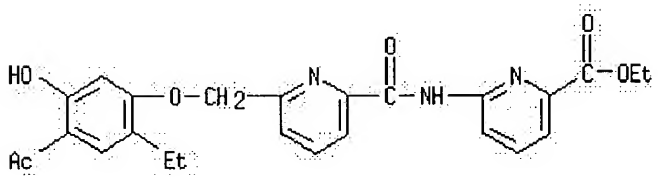



I

AB Title compds. I (A = alkylene; B, X = (substituted) phenylene, heteroarylene; Y = bond, O; Z = bond, alkylene; R1 = alkyl; R2 = OH, C1-C5 alkoxy; R3, R4 = H, alkyl, alkenyl or alkynyl; R5 = H, C1-C5 alkyl or hydroxyalkyl; R6 = (modified) carboxy; NR5R6 = heteroarom.) were prepd. as allergy inhibitors and antiinflammatories (no data). Thus, 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxylic acid, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, 1-hydroxybenzotriazole, 2-aminothiazole-4-carboxamide, and triethylamine were stirred in CH2Cl2/DMF at room temp. for 44 h to give 2-[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxamid]thiazol-4-ylcarboxamide.

IT **148350-76-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidn. of, in prepn. of leukotriene B4 antagonists)

RN 148350-76-9 HCAPLUS
CN 2-Pyridinecarboxylic acid, 6-[[[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]-2-pyridinyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

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| FULL ESTIMATED COST | 166.32 | 329.51 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -19.60 | -19.60 |

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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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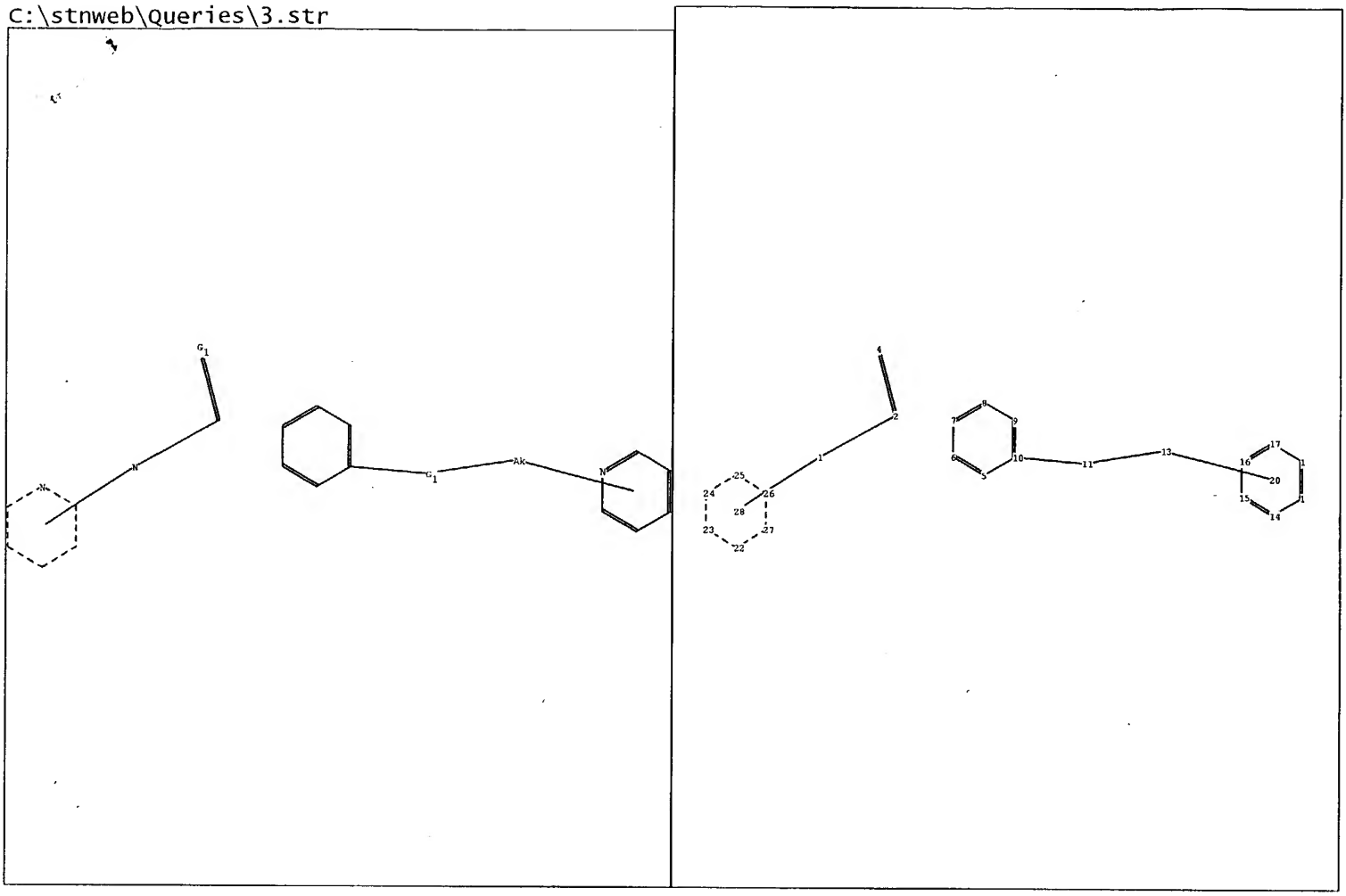

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ring nodes :
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chain bonds :
1-2 2-4 10-11 11-13
ring bonds :
5-6 5-10 6-7 7-8 8-9 9-10 14-15 14-19 15-16 16-17 17-18 18-19 22-23 22-27
23-24 24-25 25-26 26-27
exact/norm bonds :
1-2 2-4 10-11 11-13 22-23 22-27 23-24 24-25 25-26 26-27
normalized bonds :
5-6 5-10 6-7 7-8 8-9 9-10 14-15 14-19 15-16 16-17 17-18 18-19
isolated ring systems :
containing 5 : 22 :

G1:O,S

Match level :
1:CLASS 2:CLASS 4:CLASS 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS 22:Atom
23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:CLASS